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INDHOLD

Patientskole for kræftramte og pårørende

af
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Som noget nyt har vi oprettet en patientskole for kræftramte og pårørende tilknyttet onkologisk og hæmatologisk afdeling på Næstved Sygehus. Vi har, modsat mange andre steder i Danmark, hvor man har lavet patientskoler specifikt for en sygdomsgruppe, udbudt undervisning til en bred målgruppe, det vil sige, at alle patientgrupper uanset diagnose kan melde sig til skolen, og den enkelte patient har mulighed for at tage en pårørende med. Dette har vi valgt, dels fordi vores afdeling behandler patienter med mange forskellige onkologiske og hæmatologiske lidelser, og dels fordi vi har et stort optageområde, som dækker det gamle Storstrøms Amt samt halvdelen af det tidligere Vestsjællands Amt. Vores bekymring var både, om vi kunne samle deltagere nok, hvis undervisningen var tilrettelagt specifikt for en diagnosegruppe, samt om nogle deltagere ville finde afstanden for lang, f.eks. fra Nakskov til Næstved. Det har dog efterfølgende vist sig, at der var flere deltagere med bopæl langt fra Næstved.

Formålet med at oprette en patientskole har været:

- At give patienterne viden om sygdom og behandling samt om hvilke fysiske, psykiske og sociale konsekvenser, der vil være på længere sigt.
- At patienten kan blive en mere aktiv deltager i sit eget behandlingsforløb.
- At give et indblik i hvordan man kan ændre livsstil og planlægge fremtiden på en hensigtsmæssig måde.
- At give mulighed for samvær og udveksling af erfaringer med ligestillede.
- At give rådgivning og støtte fra professionelle.

Patientskolens undervisning fandt sted tre dage i september efter vores ambulatoriums lukketid, og der blev undervist i overordnede emner som kræft, behandling og bivirkninger. Desuden underviste forskellige faggrupper i psykiske reaktioner, motion, ernæring, sociale rettigheder og tilbud fra afdeling for lindrende indsats. Undervisningen foregik under afslappede forhold i et stort mødelokale, og der blev serveret sandwich og frugt i pausen, hvor deltagerne havde mulighed for at dele erfaringer. Den oprindelige tanke var, at man skulle tilmelde sig alle tre

dage, men det lykkedes også at få plads til de deltagere, som havde specifikke ønsker om bestemte emner eller som af forskellige grunde ikke kunne deltage alle tre gange. Der var stor interesse fra patienter og pårørende, og holdet blev meget hurtigt fyldt op. Da flere ikke dukkede op til den første undervisning, lavede vi overbookning på holdet, og de sidste gange var der fyldt op. Det var overvejende patienter, som deltog, men pårørende var også repræsenteret med ca. en tredjedel.

For at kunne evaluere indholdet, niveau og i det hele taget at få forslag til forbedringer, fik alle deltagere, både patienter og pårørende, udleveret et spørgeskema. For at få afklaret, hvorvidt der var grundlag for en mere specifik undervisning, blev der på evalueringsskemaet også spurgt om, hvornår man havde fået sin diagnose, og hvilken diagnose man havde. Som man kan se i tabel 1, så var det overvejende patienter med c. mamma, som deltog, men ikke nok til at oprette et specifikt hold for denne gruppe, da vores hold bestod af 25-30 deltagere. Ingen deltagere ytrede i evalueringen ønske om specifik undervisning, dog var der en enkelt, som ønskede, at holdet blev delt i deltagere, som henholdsvis var i behandling eller var færdigbehandlede.

Ud fra de evalueringer vi har fået, kan vi se, at det faglige niveau i undervisningen har været passende, og de fleste synes, at undervisningen har levet op til forventningerne.

De fleste har oplyst, at deres forventninger var at få mere viden om kræft, behandlingsmuligheder og forebyggelse. At få redskaber til at komme videre og få viden om, hvad man selv kan gøre.

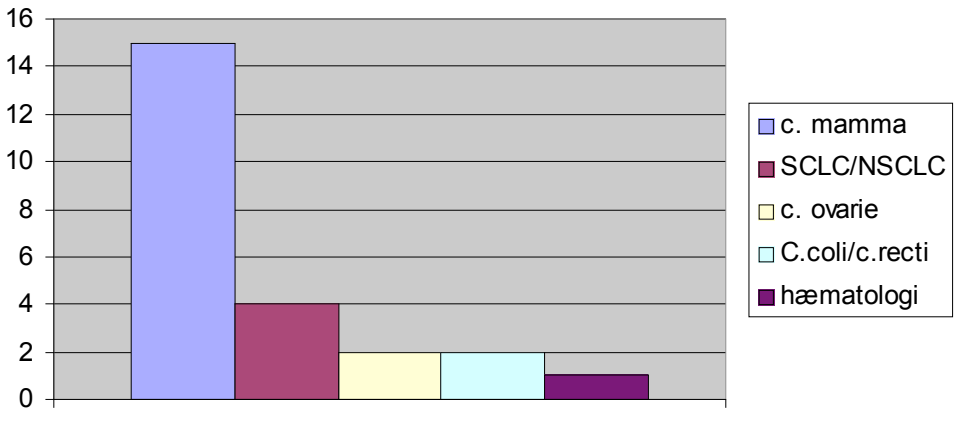
Programmet vil på baggrund af deltagernes tilbagemeldinger blive justeret inden næste patientskole. Et af ønskerne var, at der var længere pauser, da det er en vigtig del af det sociale aspekt, at deltagerne kan spørge til hinandens erfaringer og høre om hinandens velbefindende. Nogle kender jo hinanden fra venteværelset i vores ambulatorium.

Der var også ønske om at høre om stråleterapi, og hvad der sker i udlandet på området.

Der er generelt kommet mange gode tilbagemeldinger om, at indholdet i undervisningen var oplysende og berigende. Et citat fra en deltager var: "Vi vil opfordre alle med en kræftdiagnose til at deltage i eventuelt kommende undervisningstiltag." Mange har takket både mundtligt og skriftligt for et godt initiativ.

Vi må således konkludere, at behovet for undervisning er der, og at man godt kan have hold på tværs af forskellige diagnoser og tidspunkt for diagnosticering. Vi holder derfor som planlagt patientskole to gange årligt, næste gang i foråret 2009.

Antal tilmeldte patienter fordelt på diagnoser



1

Ph.D.-referat

Dendritcellevaccinationsbehandling til patienter med metastatisk renalcellecarcinom

Af
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Et stort antal dendritcelle (DC) baserede vacciner er blevet testet i kliniske fase I/II studier og nogle enkelte randomiserede fase III studier til behandling af cancerpatienter. Resultaterne fra disse studier har vist, at det er muligt at inducere et immunrespons, og at der opnås tumorregression i en mindre del af patienterne. DC vaccination er fortsat en eksperimentel behandling, og behandling med tyrosinkinasehæmmere og immunterapi med IL-2 og IFN-α er aktuelt den bedst dokumenterede behandling til patienter med metastatisk renalcellecarcinoma (mRCC). Nyere forskning har vist, at immunsuppression medieret af regulatoriske T-celler (Treg) muligvis er en af de væsentligste mekanismer bag udvikling af immuntolerance over for tumor og kan dermed være en af forhindringerne for at opnå succes med immunterapeutisk behandling til cancerpatienter.

I den første del af dette ph.d. studie blev der etableret et klinisk fase I/II forsøg med en DC-baseret vaccine kombineret med lavdosis IL-2 til behandling af patienter med mRCC. Sikkerhed og toksicitet ved behandlingen blev testet, og induktion af immunrespons, tid til progression og klinisk respons på behandlingen blev undersøgt. Desuden blev det analyseret, om serum IL-6 og YKL-40 er potentielle biomarkører ved DC vaccinationsbehandling.

Anden del af denne afhandling fokuserede på udvalgte immunsupprimerende mekanismer hos mRCC patienter, der blev behandlet med DC vaccination og lavdosis IL-2. Effekten af denne behandling på Treg celler i perifert blod hos patienter med mRCC blev undersøgt ved hjælp af multiparametrisk flow cytometri og korreleret med klinisk respons og niveauet af serum TGF-β og IL-6 under behandlingen.

Tredive patienter med mRCC i progression blev inkluderet i det kliniske fase I/II studie, og 27 af disse patienter var klinisk evaluerbare. Patienterne blev behandlet ambulant med autologe DC pulset med telomerase/survivin peptider eller tumor lysat kombineret med lav-dosis IL-2. Behandlingen var ikke forbundet med væsentlige bivirkninger. Næsten halvdelen af de behandlede patienter opnåede sygdomsstabilisering, og i mere end 1/3 af patienterne persisterede sygdomsstabiliseringen i mere end 6 måneder. Antigen specifik immunrespons blev observeret i en mindre andel af de behandlede patienter. Respons-associerede ændringer i serum IL-6 og YKL-40 blev observeret under behandlingen, og serum IL-6 og YKL-40 kan være potentielle respons biomarkører ved DC vaccinationsbehandling. Kombinationen af den opnåede immunrespons hos en del af de behandlede patien-

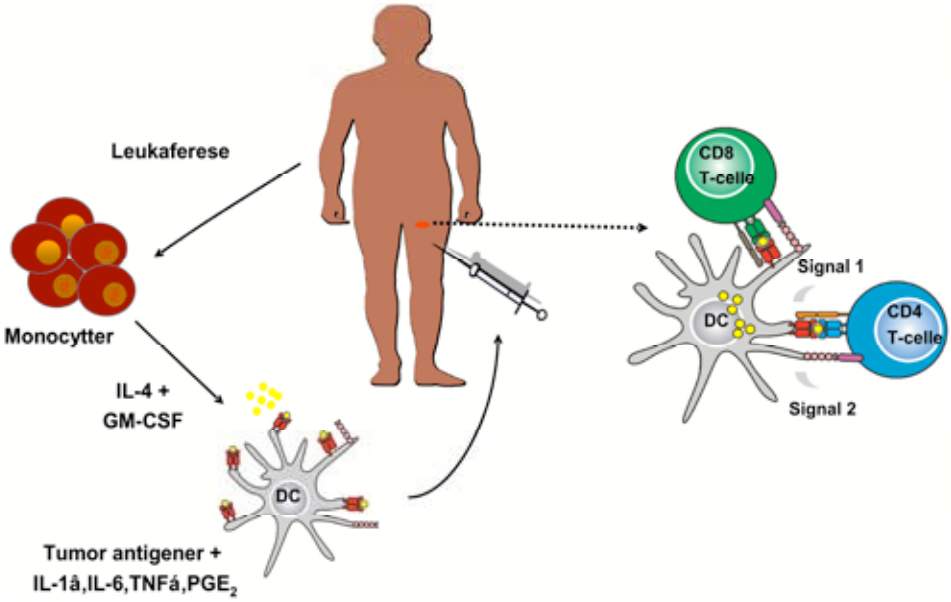


Fig.1: ***Fremstilling af dendritcellevacciner til klinisk anvendelse.*** *Monocytter isoleres fra patientens perifere blod ved leukaferese. Umodne dendritceller genereres in vitro ved tilsætning af cytokinerne IL-4 og GM-CSF. Herefter tilsættes tumor antigener og dendritcellerne opmodnes med en cocktail af cytokiner. Cellerne høstes og nedfryses og kan efter optøning administreres til patienten ved intranodal eller intradermal injektion. I lymfeknuderne præsenterer dendritcellerne tumorantigenerne for T-cellerne og inducerer derved en immunreaktion rettet mod tumorceller.*

Dendritcellevaccinationsbehandling til patienter med metastatisk renalcellecarcinom

ter, et fald i serum IL-6 hos patienter, der opnåede sygdomsstabilisering, og det faktum, at patienterne var i progression ved inklusionen i protokollen kunne tyde på, at den observerede sygdomsstabiliseringen blev induceret af vaccinationsbehandlingen. Imidlertid giver fase I/II studiedesignet ikke mulighed for at drage endelige konklusioner om klinisk effekt af behandlingen, og det er nødvendigt med yderligere studier for at afklare dette spørgsmål.

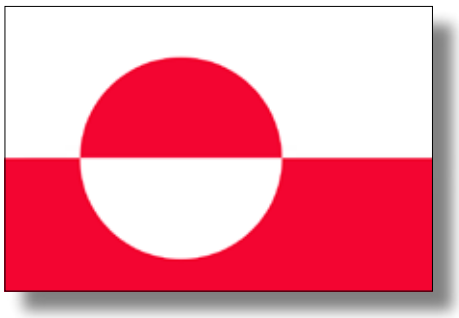
Nyere viden har vist, at immunsuppression medieret af regulatoriske T-celler muligvis er en af de væsentligste mekanismer bag udvikling af immuntolerance over for tumorer. Derfor blev ændringer i mængden af Treg celler i perifert blod undersøgt hos 25 af de behandlede mRCC patienter. Resultaterne viste, at DC vaccination kombineret med lav-dosis IL-2 giver en signifikant øgning af Treg celler i perifert blod efter 4 ugers behandling. Treg celler kan muligvis forhindre dannelsen af et effektivt immunrespons mod tumor og delvist forklare, hvorfor behandling med DC vaccination sjældent giver anledning til tumor regression. Fremtidig forskning må derfor afklare, om kombinationsbehandlinger med DC vaccination og elimination af Treg celler kan forbedre muligheden for at opnå dannelsen af et effektivt anti-tumor respons hos cancerpatienter, og dermed øge responsraterne ved DC vaccination.

På Onkologisk Afdeling, Herlev Hospital fortsætter forskningsarbejdet med dendritcellevaccination til cancerpatienter under ledelse af overlæge Inge Marie Svane. Der er aktuelt protokoller åbne for inklusion med dendritcellevaccinationsbehandling til patienter med metastatisk mammacancer i tidligt stadie, disseminеret malignt melanom og metastatisk renalcellecarcinom.

Nyt fra SKA

Nyt medlem af SKA

Det er en stor glæde at kunne byde Grønland velkommen som medlem af SKA – vi ser frem til et inspirerende samarbejde og håber, at medlemskabet vil blive til gensidig glæde.



Ph.D. referat

HER familien ved epithelial ovarie cancer - biologiske og kliniske aspekter

Af
Karina Dahl Steffensen
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Onkologisk Afd.
Vejle Sygehus

Ovariecancer er den hyppigste dødsårsag blandt de gynækologiske cancertilfælde. Symptomerne på denne form for kræft er som regel vage og uspecifikke og leder ikke umiddelbart mistanken hen på, at der kan være noget galt i underlivet. Derfor når kræften tit at sprede sig til et avanceret stadie, inden kvinderne kommer i behandling.

En sikker og specifik screeningsmetode er ikke fundet, og ovariecancer diagnosticeres derfor oftest først i et fremskredet stadie. På trods af et initialt komplet klinisk respons efter 1. linje kemoterapi får hovedparten af patienter med avanceret ovariecancer efterfølgende recidiv. Nye tiltag for at forbedre den dårlige prognose for patienter med ovariecancer involverer et behov for bedre og mere specifikke biomarkører samt nye behandlingsformer.

Molekylærbiologiske markører kan muligvis blive et nyttigt værktøj til at identificere patienternes individuelle risiko og kan således være et vigtigt redskab til identifikation af patienter, der har en særlig dårlig prognose, og som derfor skal behandles mere intensivt eller anderledes end patienter, der har en forskellig profil af biomarkører. Således kan biomarkører være med til at skræddersy behandlingen til de enkelte patienter ud fra særlige kendetegn ved patientens cancersygdom.

Dysregulering af det Humane Epidermale vækstfaktor Receptor system (HER) kendes fra flere cancerformer. HER familien består af fire medlemmer; HER1, HER2, HER3 og HER4, som er involveret i normale cellers vækst, differentiering og overlevelse. Hyperaktivering af HER systemets signalering kan ske via forskellige mekanismer. Der kan således forekomme overekspression af receptorerne eller overproduktion af ligander. Derudover kendes der flere mutationer af enten receptoren eller af de intracellulære signalveje, som bevirker, at signaleringsvejene bliver konstant aktiverede. Aktivering af tumorcelle HER proteiner kan igangsætte en kaskade af intracellulære hændelser inkluderende celleproliferation, blokeret apoptose, invasion, metastasering og tumorinduceret karnydannelse – alle de klassiske kendetegn på cancerudvikling (fig. 1).

Den epidermale vækstfaktorfamilie er således en potentiel molekylærbiologisk markør og mål for targeteret cancerterapi hos patienter med ovariecancer.

Hovedformålet med ph.d. afhandlingen var at undersøge betydningen af HER familien ved epithelial ovariecancer. Afhandlingen indbefatter en undersøgelse af HER1-4 kvantitative proteinkoncentrationer og gen ekspressionsniveauer hos benigne, borderline og maligne ovarietumorer sammenlignet med indholdet i normalt ovarievæv. Hertil er den mulige eksistens af EGFRvIII mutationen i benigne og maligne ovarietumorer undersøgt. Ydermere er flere kliniske aspekter

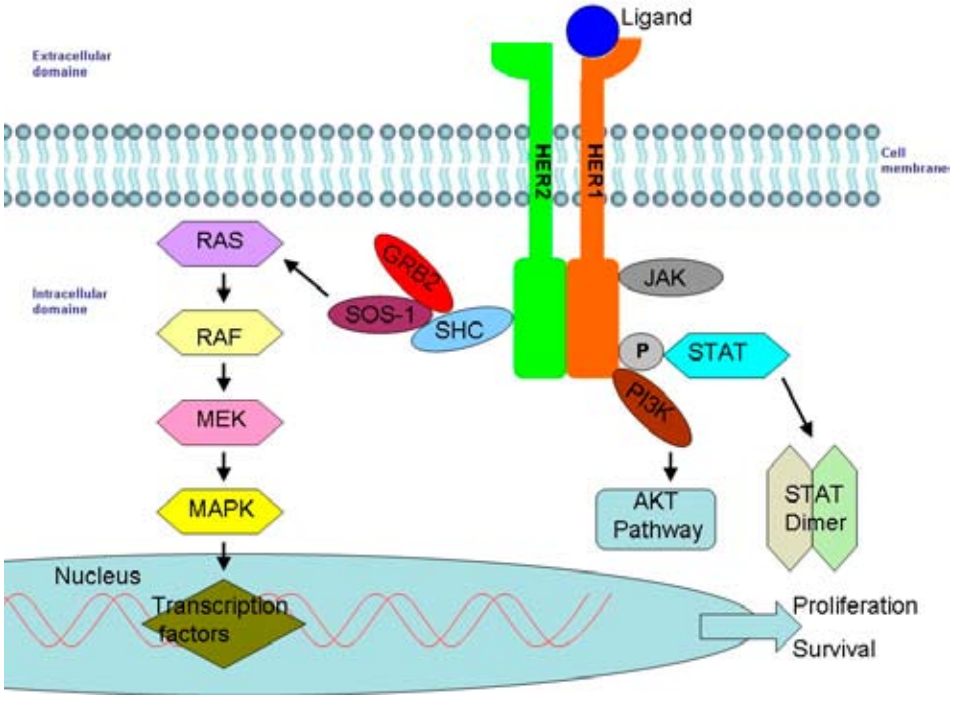

Fig. 1

undersøgt i et studie af præoperative HER1 og HER2 serum værdier. Den prognostiske signifikans af HER2 status er ligeledes undersøgt i et patientmateriale med meget lang opfølgningstid.

Afhandlingen baserer sig på 4 artikler. Artikel I illustrerer signifikant nedsat koncentration af HER1 protein og signifikant forhøjede HER2, HER3 og HER4 proteinkoncentrationer samt øgede HER2, HER3 og HER4 gen ekspressionsniveauer i ovariecancervæv sammenlignet med normalt ovarievæv og med benigne og borderline tumorer (N=207). Specielt for HER3 og HER4 var disse proteiner kun til stede i en meget lille mængde i normale og benigne ovarier og omvendt tilstede i meget større mængder i malignt ovarievæv (fig. 2A-H).

En muteret form af HER1 receptoren, EGFRvIII, som mangler en del af det ekstracellulære domæne, er blevet detekteret hos nogle tumorer. Denne muterede receptor er ikke i stand til at binde ligander, men er alligevel konstitutivt fosforyleret og aktiv. Da EGFRvIII kun er fundet i malignt væv og ikke i normalt væv, er EGFRvIII et attraktivt mål for targeteret biologisk behandling mod tumorceller uden indvirkning på normalt væv. Denne mutation er derfor yderst interessant - ikke kun fra et biologisk synspunkt, men også fra et klinisk synspunkt.

I artikel II undersøgtes den potentielle tilstedeværelse af EGFRvIII mutationen ved ovariecancer og resultaterne indikerer, at denne mutation ikke er tilstede i hverken normalt ovarievæv eller i benigne/maligne ovarietumorer (N=225) og således næppe er involveret i patogenesen af ovariecancer.

Afhandlingen indeholder desuden en undersøgelse (artikel III) af præoperative serumniveauer af HER1 og HER2 et materiale af benigne, borderline og maligne ovarietumorer (N=283).

Serum HER1 niveauet var signifikant lavere hos ovariecancerpatienter, mens kun en mindre procentdel (15.3 %) af ovariecancerpatienter havde forhøjede serum HER2 niveauer. Serum HER1 og HER2 havde høj specificitet (og høj PPV), men meget lav sensitivitet (og lav NPV) og er derfor af begrænset klinisk interesse som enkelt markører. Både RMI og CA125 var bedre til diagnostiske formål sammenlignet med HER1 og HER2.

Endelig blev den prognostiske værdi af HER2 ekspression samt sammenhængen mellem HER2 immunhistokemi (IHC) og HER2 FISH undersøgt. Resultaterne er præsenteret i artikel IV. Der blev påvist en højsignifikant korrelation mellem HER2 ekspression målt ved immunhistokemi og HER2 gen amplifikation detekteret ved FISH analyse (N=160). Derudover indikerer resultaterne, at kun en mindre del af patienter med epithelial ovariecancer udviser HER2 overekspression (IHC 2+: 6.9%, IHC3+: 4.4%).

Patienter, som var HER2 positive, havde signifikant dårligere overlevelse end patienter med HER2 negative tumorer. Mest interessant var det, at der kunne detekteres en signifikant forskel (P=0.0064) i overlevelsen mellem patienter, som var helt negative for HER2

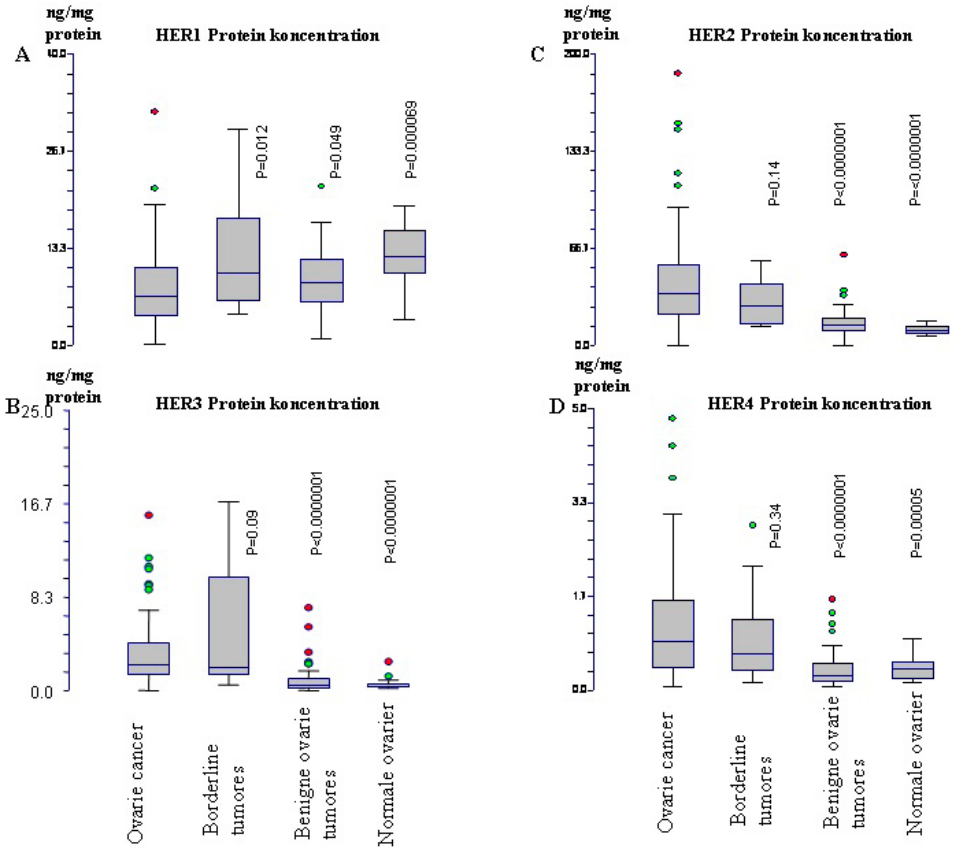

Fig. 2 A-D

(IHC 0), og patienter, som var svagt til stærk positive for HER2 (IHC 1,2,3+).

Resultaterne i denne ph.d. afhandling indikerer, at HER familien har en biologisk rolle og betydning ved epithelial ovariecancer. Ydermere har systemet formentligt også en klinisk betydning. Designet af terapeutiske stoffer rettet mod molekylære "targets" i cancerceller bør overveje forskelle i ekspressionen af "targets" i cancerceller og normale celler. Den epidermale vækstfaktor familie repræsenterer et attraktivt mål for targeteret cancer terapi, og resultaterne i denne afhandling bidrager med en rationel basis for anti-HER biologisk behandling baseret på receptorekspression. Den største udfordring for biologisk målrettet behandling er identifikationen af simple og effektive "targets". Den ideelle situation er prædiktiv test FØR målrettet behandling. Dette vil være en rational udvælgelse af den rette behandling, til den rette patient, til den rette tid. En sådan tilgang burde inkorporeres i fremtidige kliniske studier.

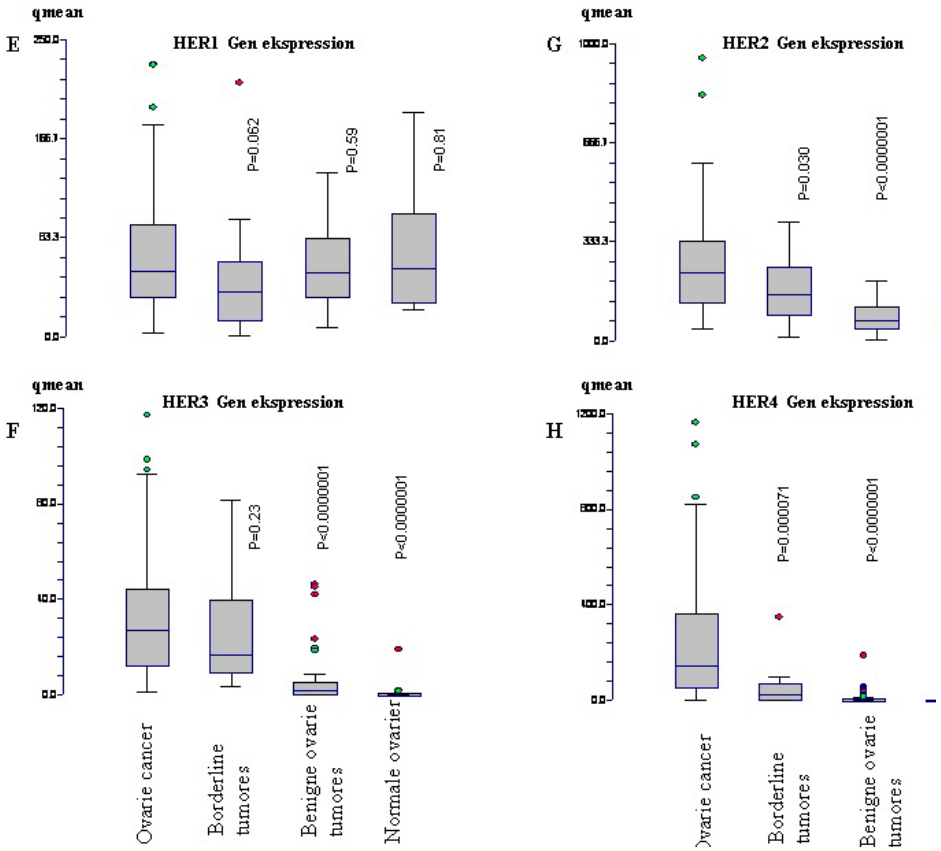

Fig. 2 E-H

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SKA

Udgives af
"Sammenslutningen af kræftafdelinger i østdanmark"
og udkommer fire gange årligt

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Møde i det Nationale Koordinationsudvalg for Eksperimentel Kræftbehandling

Uddrag af møderesumé

Seneste møde i Sundhedsstyrelsens Nationale Koordinationsudvalg for Eksperimentel Kræftbehandling, NKU, blev holdt tirsdag d. 21. oktober 2008.

Udvalget gennemgik de igangværende protokoller, jvf. Liste over behandlinger i NKU regi, november 2008, med følgende bemærkninger:

Abstract med resultaterne fra kombinationsbehandling med 3 cytostatica ved cholangiokarcinom fra Vejle og Rigshospitalet er sendt til American Society of Clinical Oncology Congress i foråret 2009, og en artikel er under forberedelse.

- Kemoembolisering ved hepatocellulært karcinom forventes indført som standardbehandling, og vil derfor blive slettet fra listen over behandlinger i NKU-regi.

- Behandling af hetapocellulært karcinom med nexavar. Ansøgning om indførelse af denne behandling som standardbehandling er under udarbejdelse. NKU anbefaler, at behandlingen derfor udfases som eksperimentel behandling pr. 31.12.08. Drøftes i Nationalt Udvalg for Kræftlægemidler (UVKL).

- Regional kemoterapi – lokalindgift af cytostatica i a. hepatica ved levermetastaser efter colorektal cancer. Protokollen fortsætter. Ny protokol er under forberedelse med Odense og Herlev som behandlingssteder. Synopsis til ny protokol vil blive forelagt på næste NKU møde.

- Kombinationsbehandling med cetuximab og irinotecan ved disseminеret colon cancer. NKU forventer, at protokollen i eksperimentelt regi lukkes pr. 31.12.08. Fortsat behandling drøftes i UVKL.

- Kombinationsbehandling med docetaxel og cisplatin ved adrenokortikalt carcinom. Protokollen forløber planmæssigt og fortsætter.

- Fase I undersøgelserne på Rigshospitalet og Herlev Hospital fortsætter.

- Behandling af cholangiokarcinom, nr. 7 og 14 på Liste over behandlinger i NKU regi, fortsætter i disse to protokoller. Patienter med K-RAS mutation behandles med 3-stof kemoterapi, mens patienter med K-RAS wild type gives 3-stof kemoterapi suppleret med Erbitux.

- Hjernetumor protokollen forløber som planlagt, og der mangler kun få patienter. Behandlingen fortsættes i ny protokol men nu med industrideltagelse, hvorfor den ikke længere kan være i NKU-regi.

- Behandling af dissemineret nyrecancer med sorafinib og sunitibin. Odense er med i denne protokol. Der er udarbejdet en MTV undersøgelse, og NKU anbefaler udfasning pr. 31.12.08. Behandlingen drøftes i UVKL.

- Behandling med avastin og carboplatin ved platinresistent epithelial ovariecancer i Vejle og på RH. 28 ptt er behandlet med avastin + enkeltstof og 4 med carboplatin og avastin.

- Behandling af dissemineret kolorektal cancer med cetuximab, irinotecan og sunitinib. Behandlingen gives til K-RAS wild type alene. Ca. halvdelen af patientantallet er indgået.

- Behandling med irinotecan og cetuximab af platinresistent esophagus- eller ventrikel cancer. RH afløser Herlev som behandlingssted, når den planlagte strukturændring i Region Hovedstaden træder i kraft.

  I alt seks protokolsynopser var indsendt til vurdering. NKU afventer protokollerne i sin helhed inden endelig stillingtagen i fem af tilfældende.

Derudover vurderede man:
Intrahepatisk kemoterapi (IHC) med oxaliplatin hver 2. uge kombineret med systemisk capecitabin og til patienter med HER2-positive tumorer desuden med trastuzumab (Herceptin) til patienter med ikke-resektable levermetastaser fra brystkræft.
- denne protokol er forud drøftet i DBCG, der er positive over for, at behandlingen initieres hurtigst muligt. NKU var enige i, at behandlingen umiddelbart kan initieres som eksperimentel behandling i henhold til de anførte indgangskriterier.

Mødereferat og "*Liste over behandlinger i NKU regi*" findes i sin helhed på *www.skaccd.org/NKU*.

Kursusreferat:

Palliation
Fokus på den onkologiske afdelings rammer og muligheder

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Tak til arrangørerne af ovennævnte kursus, der blev holdt på Hotel Kong Arthur, København, i juni 2008. Det var for mig et meget udbytterigt kursus, hvilket gav anledning til, at jeg skrev et referat fra kurset til mine kollegaer (plejepersonale, læger og sekretærer), fordi jeg lærte en masse, som jeg vurderede, de kunne have glæde af at få del i.

Referatet blev desuden sendt til arrangørerne af kurset i forbindelse med en mail, hvor deltagerne blev takket for deres aktive medvirken på kurset, hvilket i øvrigt var en fin gestus. Jeg blev herefter bedt om at skrive et notat til SKA Nyt med udgangspunkt i ovennævnte referat.

Jeg fik meget ud af kurset – enkelte nyheder inden for det faglige, men også nye ideer til forbedringer og ikke mindst var der mange interessante oplæg, der gav stof til eftertanke.

Her et par " vise" ord, som var gennemgående på kurset:

- Enkelhed i behandlingen er et godt princip
- Det er hårdere at få noget frataget (f. eks. behandlingstilbud), som man er blevet "lovet" end slet ikke at få tilbuddet
- Hvis du siger Ja til kærligheden, siger du Ja til at være medbyrdebærer
- Man kan ikke jage livsmodet, heller ikke kærligheden…..
- Afmagt er ikke at kunne se muligheder
- Afmagt er ikke at have magt til……
- OG så blev det igen slået fast for mig, at mennesker dør, som de har levet, og det betyder rigtig meget for, hvordan den palliative periode opleves af personalet, der er omkring familien
- Man kan blive smittet af såvel LIVSMODET som af AFMAGTEN – og vi skal passe på ikke af blive smittet af afmagten
- Mening – meningsløshed. Finde en mening i det og ikke en mening med det
- Mange mennesker har ikke ord for det religiøse, men det betyder ikke, at de ikke tror
- Mange mennesker har heller ikke ord for det, de føler, men det betyder ikke, at de ikke føler

Her et par eksempler på ideer fået under kurset:

Om åben henvendelse

På palliativ afdeling på Roskilde Sygehus foreligger der en liste med punkter, der kan/skal tages stilling til, før patienten får en åben henvendelse.

Palliative patienter, der udskrives til pleje i eget hjem eller på plejehjem får en "Tryghedskuffert" med hjem. Den indeholder medicin til mulige symptomer, der kan opstå, og tilsvarende lægeordinationer til hjemmeplejen.

Og så kom psykologen og overskriften var Livsmod og afmagt

God undervisning, men svær at referere fra. Han henviste til 2 begreber, som gjorde det noget nemmere for mig at forstå, hvad der sommetider foregår i de kræftramte familier. Der er 2 forskellige slags kærlighed:

- AGAPE, som er den kærlighed, der går i ynglens lige linje (forældre – barn, barn – forældre etc)
- EROS, som er den kærlighed, der opstår mellem "kærester", mand – kone

Dette er 2 forskellig slags kærlighed, som det er vigtigt at skille ad. Artikel om dette blev eftersendt af psykologen (Kærlighedens natur af Erik Schultz).

Og så kom præsten

- Kærligheden er stærk som døden
- Kærligheden er stærkere end døden – det betyder at netop derfor huskes den, man elsker efter døden, og det kan være en trøst for den døende – alle mennesker vil gerne sætte sig spor, så de huskes efter de er døde.
- "Ikke at blive set" er slemt…….

Om Egmontsfondens Børne og Ungdomsrådgivning

Et rigtig dejligt foredrag af en af psykologerne herfra. Vi blev lige mindet om at:

- Børn registrerer alt, derfor information. Børnenes fantasi er uden grænser, og det er slemt at høre udefra, at ens mor/far/søskende er alvorligt syg "Hvordan kan det være, at det er vigtigere at fortælle det til andre frem for mig?"
- Alvorlig krise/sygdom i en familie kan give "opdragelsespauser", men det er skidt, da børnene netop i disse situationer har brug for

C-vitamin

Vitamin C hæmmer cytostatikas effekt ved hyperpolarisering af mitochondrierne

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I september udgaven af SKA nyt kunne man læse et glimrende indlæg af Martin Hutching, som frarådede brugen af antioxidanter i forbindelse med onkologisk behandling. Anbefalingen var baseret på en nyere artikel i JNCI, der systematisk gennemgår klinisk kontrollerede forsøg på området. Hovedvægten lå på vitamin Cs virkning som antioxidant, der menes at hæmme frie radikaler. Sidstnævnte dannes f.eks. ved kemo- og stråleterapi og resulterer i apoptose.

I forlængelse heraf er der publiceret en artikel i Cancer Research fra oktober 2008, der elegant underbygger ovenstående postulat i et præklinisk - kombineret *in vitro* og *in vivo* - studie, som fremsætter nye hypoteser omkring årsagerne til vitamin Cs antagonistiske virkning til kemoterapi.

Man undersøgte dehydroascorbinsyres effekt på CML og lymfomcellelinier samt i mus med lymfom. Mus og celler blev behandlet med forskellige cytostatika, som feks Vincristin, Cisplatin, Metotrexat og Imatinib. Stofferne varierer som bekendt betydeligt i virkningsmekanisme. Man fandt, at følgende gjorde sig gældende for vitamin C:

1. Beskyttede cellelinierne mod diverse cytostatika, uanset stofgruppe.
2. Antagoniserede doxorubicin *in vivo*, intracellulært.
3. Hæmmede apoptose-tendensen mellem 37% - 82% *in vitro*.
4. Medførte kun diskret reduktion af intracellulære niveauer af frie radikaler
5. Hyperpolariserede mitochondriernes cellemembran.

Det var ganske overraskende, at vitamin C antagoniserede så forskellige cytostatika på trods af en kun lille reduktion af intracellulære niveauer af frie radikaler. Sidstnævnte fakta har tidligere været mistænkt for at være hovedmekanismen bag vitamin Cs antagonistiske effekt. Man ved, at mitochondriemembranens depolarisering er stærkt involveret i apoptose, som muligvis mange cytostatika påvirker, og som vitamin C således hæmmer.

Konklusivt kan man altså fortsat fraråde kræftpatienter, der får kemoterapi, at bruge højdosis C-vitamin som kosttilskud. Man skal dog bære in mente, at resultaterne bygger på leukæmi- og lymfomcellelinjer samt mus. Det virker dog usandsynligt, at effekten af vitamin C er begrænset til specifikke hæmatologiske/onkologiske sygdomme, og mange af effekterne relaterer til den overordnede cellecyklus. En ting er dog sikkert: man kan ikke overføre data fra mus til mennesker, desværre…

Reference:
Heaney M, Gardner J, Karasavvas N et al. Vitamin C antagonizes the cytotoxic effect of antineoplastic drugs. Cancer Res 2008;68:(19). October 1.

... fortsat fra forrige side

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rammer, struktur, og at der stilles de samme krav som sædvanlig

- Børnene har brug for at vide, om symptomer er alvorlige eller ikke alvorlige
- Børnene ved altid, hvordan forældrene har det
- Børn kan reagere på truslen om tab ved at holde op med at lære.

Om "gørelse" og "værelse"

Jeg lærte to nye begreber af en sygeplejerske (fra Esbjerg). Da vi talte om, hvad vi kunne gøre i forskellige vanskelige situationer, sagde hun "Det handler måske ikke altid så meget om "gørelse" - men om "værelse".

33. ESMO Kongres, Stockholm, 12-16. september 2008

PHASE (PH) I/II STUDY OF THE HISTONE DEACETYLASE INHIBITOR BELINOSTAT (BEL) IN COMBINATION WITH CARBOPLATIN (CA) AND PACLITAXEL (P) IN ADVANCED SOLID TUMORS (PH I) AND RELAPSED OVARIAN CANCER(PH II)

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Bel is synergistic with Ca and P in preclinical models, including ovarian cancer. This study assesses safety and activity of the BelCaP combination

Methods:

In ph I, cohorts of 3-6 patients (pts) were treated with escalating doses of Belas a 30-min infusion daily for 5 days (d) together with standard dose Ca and/or P(on d 3) every 3 weeks. In ph II, pts were treated with Bel 1000 mg/m2/d, d 1-5, CaAUC 5 d 3, and P 175 mg/m2 d 3.Results: In ph I, 23 pts were treated with a median of 4 cycles (range 1 – 28+) in 3 cohorts with Bel 600 mg/m2/d (BelCa, BelP, BelCaP), and BelCaP with Bel 800 and1000 mg/m2/d. No dose-limiting toxicity was observed. Drug-related adverse events(AE) were nausea and fatigue with no related grade 4 AE, and grade 3 non-hematological AE in more than one pt was peripheral sensory neuropathy (n=2). Most common grade 3/4 laboratory abnormality was neutropenia (26% of pts). 2 pts hadpartial responses (PR): 1 with rectal cancer (3 prior therapy lines) and 1 with pancreatic cancer (prior gemcitabine). Median treatment duration for 11 pts with stable disease (SD) was 116 d (range 43 to +592 d); 4 pts received > 10 cycles (unknownprimary, bladder, melanoma, Ewings sarcoma).Ph II enrolled 35 patients with epithelial ovarian cancer (median 3 prior regimens;range 1-4). Recruitment was completed in Dec 2007 with 11 pts currently on therapy. Most common related AE were nausea (80%), fatigue (73%), vomiting (63%), and diarrhea (27%); most common related grade 3/4 AE were neutropenia (n=4),transaminitis (n=4), and fatigue (n=3). Preliminary efficacy, defining platinum sensitivity by most recently received platinum therapy, include 4 PR and 12 SD in platinum-resistant pts with platinum-free interval (PFI) < 6 mo (n=21); in the subgroup with PFI < 3 mo (n=13), there were 2 PR and 8 SD. There was 1 CR and 9 PR in platinum-sensitive pts with PFI > 6 mo (n=14). In total, 1 CR and 13 PR have been observed.

Conclusions:

BelCaP is well-tolerated and shows clinical activity in heavily pre-treated pts with advanced solid tumors, as well as in pts with platinum-sensitive and resistant ovarian cancer.

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EFFICACY AND SAFETY OF DEGARELIX VERSUS LEUPROLIDE DEPOT (7.5MG) IN A 12-MONTH, RANDOMIZED, OPEN-LABEL, PHASE III STUDY IN PATIENTS WITH PROSTATE CANCER

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Objective:

Gonadotropin-releasing hormone (GnRH) receptor blockers rapidly suppress serum testosterone (T) levels, but without the initial T surge observed with GnRH agonists. The efficacy and safety of degarelix, a new GnRH receptor blocker, was compared with leuprolide in a 12-month, open-label study in patients with prostate cancer.

Methods:

610 patients with adenocarcinoma of the prostate for whom ADT was indicated (except neoadjuvant hormonal treatment), were randomised to: degarelixstarting dose 240 mg s.c. (40 mg/mL) for 1 month followed by monthly maintenance doses of 160 mg s.c. (40 mg/mL; Group A, n=202) or 80 mg s.c. (20 mg/mL; Group B,n=207), or monthly i.m. injections of leuprolide depot 7.5 mg (Group C, n=201).

Results:

Baseline characteristics were similar across groups (mean age 72 yrs; median T3.93 ng/mL; median prostate-specific antigen [PSA] 19.0 ng/mL). At Day 3, T levelswere £0.5 ng/mL in 95.5% and 96.1% of patients on degarelix (A and B) and 0% ofpatients on leuprolide (C); at Day 14 these values were 99.5%, 100% and 18.2%. Nodegarelix patients vs 80% leuprolide-treated patients experienced a T surge (i.e. a Tincrease of ‡15% from baseline on any 2 days during the first 2 weeks' treatment). After 14 days' treatment, median PSA levels declined by 65%, 64% and 18% in Groups A, Band C, respectively. Degarelix demonstrated non-inferiority vs leuprolide at achieving the primary endpoint (attainment of serum T levels £0.5 ng/mL during monthlymeasurements from Day 28 through Day 364): 98.3%, 97.2% and 96.4% of patients inGroups A, B and C, respectively, achieved the primary endpoint. Safety profiles were as expected and mainly related to hormonal effects and disease. Disease-related sideeffects were more commonly reported with the agonist. A total of 24, 21 and 28 patientsin Groups A, B and C, respectively, experienced serious adverse events; 4, 5 and 9 patients died.

Conclusion:

Degarelix reduces testosterone and PSA significantly faster than leuprolide; without a testosterone surge. Testosterone was reduced to very low levels and degarelix was at least as effective as leuprolide in maintaining serum T levels £0.5 ng/mL for the duration of the study.

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MULTICENTRE PHASE III TRIAL COMPARING VINFLUNINE (V) PLUS BEST SUPPORTIVE CARE (BSC) VS BSC ALONE AS 2ND LINE THERAPY AFTER A PLATINUM-CONTAINING REGIMEN, IN ADVANCED TRANSITIONAL CELL CARCINOMA OF THE UROTHELIUM (TCCU)

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Background:
Second line therapy in TCCU is an unmet medical need. V is a new microtubule inhibitor that has shown in phase II trials to be active against TCCU(Culine S 2006).
Methods:
Pts were randomised (2:1) to receive V (PS 0: 320 mg/m2 q3w; PS 0 with-previous pelvic radiation and PS1: 280 mg/m2 subsequently escalated to 320 mg/m2) +BSC or BSC alone. Pts under BSC were allowed to receive chemotherapy uponprogression, other treatments as radiotherapy were permitted.
Results:
From 05/03 to 08/06, 370 pts were enrolled (253/117), 79% men; median age 64 y; PS 0/1: 31%/68%; visceral involvement: 74%. Both arms were well balanced except PS 1: 10% difference favouring BSC; Median number of cycles 4 [1-15]. Grade3/4 toxicities for V : neutropenia (50%), febrile neutropenia (6%), anemia (19%),thrombocytopenia (6%), fatigue (28%), constipation (20%), abdominal pain (9%), vomiting (4%) and peripheral neuropathy (1%). Grade 1/2 alopecia (33%) and injection site reactions (18%). There was 1 case of fatal pancytopenia. In the ITT analysis the objective of a median 2-mo survival advantage (6.9 vs 4.6 mo), favouring V+BSC was achieved, (HR 95% CI: 0.88 [0.69-1.12]) but was not statistically significant (p=.29).

The planned multivariate analysis adjusting for prognostic factors showed statistically significant effect of V+BSC on OS (p=.036); V+BSC reduced the risk of death by 23% vs BSC, (HR: 0.77 [0.61-0.98]). In the 357 pts eligible or in the 351 per protocol subjects (5 not treated and 14 major violations), OS was significantly longer for V+BSC: 6.9 vs 4.3 mo, (HR: 0.78 [0.61-0.99]; p=.04) and (HR: 0.75 [0.59-0.96];p=.02), respectively. ORR, disease control, PFS were all statistically significant favouring V+BSC (p=.0002, p<.0001, p<.001, respectively). The clinical benefit response rate was not statistically different between both arms (p<.001. V+BSC did not show an impairment of HRQL, although at week 18 V+BSC showed an improvement in HRQL when compared with BSC.
Conclusions:
Vinflunine is the first agent to demonstrate a survival advantage in 2nd line treatment for advanced TCCU. These results and their consistency may contribute to establishing Vinflunine as standard 2nd line treatment.

PACLITAXEL, CISPLATIN AND GEMCITABINE IN THE TREATMENT OF CARCINOMAS OF UNKNOWN PRIMARY SITE, A PHASE II STUDY

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Background:
Cancer of unknown primary (CUP) site represents up to 5 % of all cancer diagnoses and for this group of patients there is no standard treatment. Platinum-based regimens have shown higher response rates than non-platinum containing regimens (30-50 % vs. 20-30 %). The present study was conducted to evaluate the efficacy and toxicity of the combination of cisplatin, gemcitabine and paclitaxel in patients with CUP.
Methods:
Patients with CUP, ECOG performance status 0-1 and age between 18 and 65 years old were treated with paclitaxel 175 mg/m2 day 1, cisplatin 75 mg/m2 day 1 and gemcitabine 1000 mg/m2 day 1 and 8 in a three-week schedule.
Results:
Eighty-seven patients were enrolled between 1998 and 2007 at Rigshospitalet, Copenhagen University Hospital, Denmark. All patients were evaluable for toxicity and79 patients were assessable for response. The median age was 55 years (range 27-65)and 52 % were men. The histology of the tumours was 69 % adenocarcinomas, 7 % squamous cell carcinomas and 24 % undifferentiated carcinomas. The median number of cycles was six (range 1-12). The response rates were 3.8 % complete responses (CR) and 43.0 % partial responses (PR), resulting in an overall response rate of 46.8 %. The median survival time was 9.1 months (0-111+ months) and the survival rates at 1 and 2 years were 34.5 % and 12.6 %, respectively. The most frequent grade 3 or more adverse events were neutropenia and thrombocytopenia. There were two treatment-related deaths (1 acute renal failure, 1 febrile neutropenia).

Conclusions:
The combination of paclitaxel, cisplatin and gemcitabine is an active regimen in patients with carcinoma of unknown primary site. The treatment was well tolerated by most patients, but neutropenia and thrombocytopenia were quite common. The results in this study are comparable with other platinum- and taxane containing regimens. It is continuously important to pursue additional therapeutic trials, including randomised, as well as explore targeted biologic agents in combination with chemotherapy in this heterogeneous group of patients. Gene expression profiling may be useful in assigning the primary site. In addition, it may give a more thorough understanding of the biology of CUP as well as reveal new therapeutic targets.

33. ESMO Kongres, Stockholm, 12-16. september 2008

EFFICACY OF INTRANASAL FENTANYL FOR BREAKTHROUGH PAIN IN PATIENTS WITH CANCER: RESULTS OF A PHASE III TRIAL

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Purpose of the study:
To confirm the efficacy of intranasal fentanyl titrated to doses of 50, 100, and 200 lg, for the treatment of breakthrough pain in patients with cancer, and to establish the long-term safety of treatment with this agent, during an open-label follow-up safety period.
Methods:
A randomised, double-blind, placebo-controlled, cross-over, multi-centre trial to confirm the efficacy and safety of intranasal fentanyl titrated to doses of 50, 100, and 200 lg in the treatment of episodes of breakthrough pain. All enrolled (N=120) were cancer patients receiving chronic opioid treatment equivalent to 60–500 mg oral morphine/day or to 25–200 lg/hr transdermal fentanyl and experiencing ‡3 BTP episodes per week and £4 per day. Following titration to a dose providing pain relief within 10 min, from 50, 100, or 200 lg of intranasal fentanyl per administration, patients then received the appropriate dose in a randomised, double-blinded sequence for six of eight breakthrough pain episodes (maximum four/day) and placebo for one breakthrough pain episode each of episodes 1–4 and 5–8, respectively. Rescue analgesic after 20 minutes of treatment was permitted for patients with no or inadequate pain relief.
Results:
Of the 120 enrolled patients, 113 were randomised, 111 received intranasal fentanyl (50 lg, n = 18; 100 lg, n = 48; 200 lg, n = 55), and constituted the intent-totreat(ITT) population. Pain intensity difference at 10 minutes post dosing (PID10) was significantly higher (ranging from 2.00 to 2.74) for all doses of intranasal fentanyl, and therefore provided better pain relief, compared with placebo (overall mean, 2.56 vs.1.28, respectively, 95% CI: 1.03–1.48; $p < 0.001$). In addition the mean overall responder rate with intranasal fentanyl was more than double that observed with placebo (51% vs. 21%, respectively). The incidence of adverse events was low, and none of the serious adverse events reported were considered related to intranasal fentanyl, being mainly malignant neoplasm progression.
Conclusions:
Intranasal fentanyl at doses of 50, 100 and 200 lg were effective in treating breakthrough pain in opioid-tolerant cancer patients. All doses were shown to be safe, well tolerated, and clinically relevant.

NORDIC OBSERVATIONAL STUDY EVALUATING SAFETY AND ANALGESIC USE IN PATIENTS WITH ADVANCED CANCER UNDER ZOLEDRONIC ACID TREATMENT – INTERIM ANALYSIS L

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Zoledronic acid (Zometa_) is a bisphosphonate that has demonstrated therapeutic efficacy in a variety of solid tumours. The objectives of this ongoing study are to evaluate the safety and efficacy of treatment in patients with advanced cancer in a naturalistic setting enabling comparisons between different cancer types within the same study. 172 patients with prostate cancer (mean age 72 years), 86 patients with breast cancer (61 years) and 12 patients with lung cancer (63 years) included at 60 hospitals in Denmark, Norway and Sweden have been followed for at least 6 months. The occurrence of adverse events and skeletal related events (SREs), use of analgesics and pain were registered. Analgesic treatment was expressed as analgesic score(0= none to 4 = strong narcotics). Pain was assessed on a Visual Analogue Scale (VAS) where 0 = no pain and 100 = worst possible pain. Time from confirmed bone metastasis until start of treatment was 14.8, 9.0 and 2.3 months for prostate, breast cancer and lung cancer patients, respectively. However, variation between countries was observed. The most common SRE was radiotherapy to bone, occurring among 6% of the prostate and breast cancer patients. Analgesic score increased from an average of 1.6 to 1.9 both for prostate and breast cancer patients, whereas there was a decrease from 3.2 to 3.0 for lung cancer patients. Despite these not clinically relevant changes in analgesic use, VAS pain score decreased from an average of 38 to 13 among lung cancer patients, from 19 to 16 among prostate cancer patients and from 27 to 16 among breast cancer patients. At 9 months VAS pain score had decreased with 31.3, 2.1 and 8.3 while the analgesic score had decreased with 0.4, increased with 0.5 and 0.4 for lung, prostate and breast cancer, respectively. No clinically relevant deviations from the known safety profile of zoledronic acid were observed. Zoledronic acid is able to decrease the pain in advanced prostate, breast and lung cancer patients without any major clinical relevant increase of analgesic treatment. This study confirms the safety profile of zoledronic acid known from clinical trials and no osteonecrosis of the jaw have been reported.

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TOLERABILITY AND SAFETY OF INTRANASAL FENTANYL TREATMENT FOR BREAKTHROUGH PAIN IN PATIENTS WITH CANCER: FOUR-MONTH FOLLOW-UP

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Purpose of the study:
To confirm the long-term tolerability and safety of treatment with intranasal fentanyl titrated to doses of 50, 100, and 200 lg, for the treatment of breakthrough pain in patients with cancer, during an open-label follow-up safety period.
Methods:
This was a randomised double-blind, placebo-controlled, cross-over, multicentretrial involving 120 adult in/out patients with cancer, receiving stable, chronicopioid therapy and experiencing ‡3 BTP episodes per week and £4 per day. Patients were titrated to an effective dose (providing pain relief within 10 min) of 50, 100, or 200 lg of intranasal fentanyl per administration. Subsequently, they received their successful treatment dose of intranasal fentanyl (in a randomised, double blinded sequence), for six of eight breakthrough pain episodes (maximum four per day), and placebo for one breakthrough pain episode each of episodes 1–4 and 5–8, respectively. Rescue analgesic after 20 minutes of treatment was permitted for patients with no or inadequate pain relief. Patients were monitored for safety for 4 months after inclusion of the last patient in the trial.
Results:
In 108 patients, the mean number of days of exposure to intranasal fentanyl was 106.4 (median 86, range 1–357 days) for the safety, follow-up phase.
Sixty-five patients (60.2%) experienced adverse events (AEs) during this period: 52 (48.1%) had serious AEs, 42 (38.9%) died and 44 patients (40.7%) discontinued trial due to AEs, mainly due to progression of malignant neoplasm and unrelated to study medication. Only five patients experienced AEs considered to be related to trial drug (4.6% of all patients): five had nausea; four had constipation; two experienced vomiting, and one had epistaxis, all of which were graded mild or moderate, and one patient experienced severe dysgeusia (taste disturbance) who discontinued participation in the trial.
Conclusions:
All doses of intranasal fentanyl were shown to be safe and well tolerated. The majority of those AEs considered related to study drug were mild to moderate, and most reported AEs were considered to be related to progression of patients' underlying disease.

TITRATION OF INTRANASAL FENTANYL FOR BREAKTHROUGH PAIN IN PATIENTS WITH CANCER: EVIDENCE FOR DOSE PROPORTIONALITY VS. BACKGROUND ANALGESIA

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Purpose of the study:
To establish an effective dose of intranasal fentanyl for relief of breakthrough pain episodes in patients with cancer, prior to further confirmation of the efficacy of doses of 50, 100, and 200 lg.
Methods:
A randomised, double-blind, placebo-controlled, cross-over, multi-centre trial to confirm the efficacy and safety of intranasal fentanyl, following an initial dosefinding titration period. All enrolled patients were receiving chronic opioid treatment equivalent to 60–500 mg oral morphine/day or to 25–200 lg/hr transdermal fentanyl and experiencing ‡3 BTP episodes/week and £4 episodes/day. Titration from a 50 lg dose was achieved by patients recording the global impression (GI) score of the medication 60 min after administration of medication using a categorical five point VRS (0 = poor to 4 = excellent). Doses were considered successful if patients had (i) no need of rescue analgesia within 60 min after first administration (ii) rated GI ‡2 by 60 min after first administration (iii) experienced no severe undesirable effects (pronounced hyperventilation, unacceptable drowsiness, etc.).
Results:
Among 120 patients enrolled, 112 were titrated: 96 patients (85.7%) were titrated to 100 lg or 200 lg doses and 16 patients to the 50 lg dose; none were down titrated. In patients receiving low dose opioids for background pain medication (£180mg/day, n = 75), 15 (20.0%) were titrated to 50 lg, 37 (49.3%) to 100 lg and 23(30.7%) to 200 lg, compared with 2 (8.7%), 7 (30.4%), 14 (60.9%) for those receiving medium opioid background medication (>180–£360 mg/day, n = 23) respectively. In those receiving high opioid background medication (>360 mg/day, n = 13) 5 (38.5%) were titrated to 100 lg and 7 (53.8%) to 200 lg; and for one patient there was no titration phase. Exposure to drug ranged 2–70 days (median of 5 days, mean of 8.3 days).
Conclusions:
Generally, patients with low dose background pain treatment tended to achieve effective pain relief with a correspondingly lower intranasal fentanyl dose compared with those taking higher dose levels for background pain, and most obviously for those ending on 50 lg. All doses were shown to be safe, well tolerated, and clinically relevant.

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RANDOMIZED, DOUBLE-BLIND, PHASE III TRIAL OF STANDARD ANTIEMETIC THERAPY COMBINED WITH A SINGLE ORAL, A 3-DAY ORAL, OR A 3-DAY IV/ORAL REGIMEN OF CASOPITANT, A NOVEL NEUROKININ-1 (NK-1) RECEPTOR ANTAGONIST, IN PATIENTS (PTS) RECEIVING MODERATELY EMETOGENIC CHEMOTHERAPY (MEC)

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Background:
Casopitant, a novel NK-1 receptor antagonist, demonstrated antiemetic efficacy in pts receiving MEC in a phase II trial. Here, we report on pts receiving different regimens of casopitant in combination with ondansetron/dexamethasone(OND/DEX) for the prevention of chemotherapy-induced nausea and vomiting(CINV) due to an anthracycline and cyclophosphamide (AC)-based regimen.
Methods:
Multinational, double-blind trial enrolling 1933 pts with breast cancer (96%). All pts received DEX 8 mg IV on D1 and OND 8 mg BID PO D1-3. Pts were randomized to receive in addition either placebo (CTRL), a single oral dose (150 mg PO D1) of casopitant (CAS1), a 3-day oral (150 mg PO D1 + 50 mg PO D2-3) casopitantregimen (CAS3), or a 3-day IV/oral (90 mg IV D1 + 50 mg PO D2-3) casopitant regimen(CAS IV/PO) for up to 4 cycles. The primary endpoint was complete response (CR; no vomiting/no retching, no rescue medications) in the first 120 hrs after MEC.
Results:
CAS1, CAS3, and CAS IV/PO plus OND/DEX produced statistically significant improvements in CR rates compared with CTRL (73%, 73%, 74% vs 59% [P<0.0001 for all comparisons] respectively), and this benefit appeared to be maintained in cycles 2-4. Improvement in the secondary endpoint of no vomiting was also observed. Casopitant was generally well tolerated with AE frequency similar across arms. Common AEs were neutropenia, alopecia, fatigue, leukopenia, and constipation; injection site reactions were infrequent but slightly more common in the IV/oral arm.
Conclusion:
Addition of a CAS1, CAS3, or CAS IV/PO regimen toOND/DEX achieved statistically significant improvements in CR over 5 days compared to CTRL. All casopitant regimens were generally well tolerated and reduced emetic events experienced by pts receiving up to four cycles of MEC (Table omitted).

TITRATION OF INTRANASAL FENTANYL FOR BREAKTHROUGH PAIN IN PATIENTS WITH CANCER: EVIDENCE FOR DOSE PROPORTIONALITY VS. BACKGROUND ANALGESIA

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Purpose of the study:
To establish an effective dose of intranasal fentanyl for relief of breakthrough pain episodes in patients with cancer, prior to further confirmation of the efficacy of doses of 50, 100, and 200 lg.
Methods:
A randomised, double-blind, placebo-controlled, cross-over, multi-centre trial to confirm the efficacy and safety of intranasal fentanyl, following an initial dosefinding titration period. All enrolled patients were receiving chronic opioid treatment equivalent to 60–500 mg oral morphine/day or to 25–200 lg/hr transdermal fentanyl and experiencing ‡3 BTP episodes/week and £4 episodes/day. Titration from a 50 lg dose was achieved by patients recording the global impression (GI) score of the medication 60 min after administration of medication using a categorical five point VRS (0 = poor to 4 = excellent). Doses were considered successful if patients had (i) no need of rescue analgesia within 60 min after first administration (ii) rated GI ‡2 by 60 min after first administration (iii) experienced no severe undesirable effects (pronounced hyperventilation, unacceptable drowsiness, etc.).
Results:
Among 120 patients enrolled, 112 were titrated: 96 patients (85.7%) were titrated to 100 lg or 200 lg doses and 16 patients to the 50 lg dose; none were down titrated. In patients receiving low dose opioids for background pain medication (£180mg/day, n = 75), 15 (20.0%) were titrated to 50 lg, 37 (49.3%) to 100 lg and 23(30.7%) to 200 lg, compared with 2 (8.7%), 7 (30.4%), 14 (60.9%) for those receiving medium opioid background medication (>180–£360 mg/day, n = 23) respectively. In those receiving high opioid background medication (>360 mg/day, n = 13) 5 (38.5%) were titrated to 100 lg and 7 (53.8%) to 200 lg; and for one patient there was no titration phase. Exposure to drug ranged 2–70 days (median of 5 days, mean of 8.3 days).
Conclusions:
Generally, patients with low dose background pain treatment tended to achieve effective pain relief with a correspondingly lower intranasal fentanyl dose compared with those taking higher dose levels for background pain, and most obviously for those ending on 50 lg. All doses were shown to be safe, well tolerated, and clinically relevant.

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PHASE III RESULTS OF A SINGLE ORAL AND A 3-DAY IV/ORAL DOSING REGIMEN FOR THE NOVEL NEUROKININ-1(NK-1) RECEPTOR ANTAGONIST, CASPOPITANT (CAS), IN THE PREVENTION OF CINV IN PATIENTS (PTS) RECEIVING HIGHLY EMETOGENIC CHEMOTHERAPY (HEC)

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Background:
CAS, a novel NK-1 receptor antagonist, demonstrated efficacy in preventing CINV after HEC in a ph II trial. Here, we report a ph III trial evaluating single oral dose and 3-day IV/oral dosing CAS regimens with ondansetron/dexamethasone (OND/DEX) for the prevention of CINV in pts receiving HEC.
Methods:
This multinational, double-blind, active-controlled trial enrolled 810 pts (99% received cisplatin-based HEC regimens up to 6 cycles). Pts were randomized to an active control regimen (OND 32 mg IV and DEX 20 mg PO on D1; DEX 8 mg PO BID D2-4) (CTRL/H), a single oral dose CAS regimen (OND 32 mg IV, DEX12 mg PO and CAS 150 mg PO D1; DEX 8 mg PO BID D2-4) (CAS1/H) or a 3-day IV/oral CAS regimen (OND 32 mg IV, DEX 12 mg PO, and CAS 90 mg IV D1; DEX 8 mg PO QD D2-4 and CAS 50 mg PO D2-3) (CAS IV/PO/H) for up to 6 cycles. DEX doses were adjusted for CAS interaction. Complete response (CR; no vomiting/no retching, no rescue medications) in the first 120 hrs after HEC was the primary endpoint.
Results:
CAS1/H and CAS/IV/PO/H regimens had statistically significant improvements in CR rates compared to CTRL/H (86% and 80% vs 66% [P<0.0001,P=0.0004], respectively), which were maintained in cycles 2-6. Secondary endpoints of acute and delayed CR, no vomiting, and no nausea (VAS £5 mm) were also improved. CAS was generally well tolerated with similar AE frequency across arms. Neutropenia, leucopenia, and anemia were the most common AEs, with neutropenia and injection site reactions slightly more common in the CAS/IV/PO/H arm.
Conclusion:
Both single oral dose and 3-day regimens of CAS with OND/DEX provided statistically significant improvements in CR, resulted in reductions in acute and delayed CINV events, and were generally well tolerated (Table omitted).

TRANSFUSION USE AMONG CANCER PATIENTS: A POPULATION-BASED COHORT STUDY

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Background:
Cancer patients experience anaemia and thrombocytopenia due to underlying disease complications or as a side-effect of myelosuppressive treatment and surgery. Red blood cell (RBC) and platelet transfusions can alleviate symptoms. However population based data on transfusion use among cancer patients are sparse.
Objectives:
To examine RBC and platelet transfusion use of incident cancer patients within four months after diagnosis.
Methods:
We identified all incident cancer patients in Northern Denmark (total population ' 1.2 million), between 1998 and 2004. From population-based medical databases we obtained data on all RBC and platelet transfusions given to the patients within four months of the date of admission with cancer. Overall use of transfusions and use by age at diagnosis, cancer treatment, site and stage of disease was assessed. Results are presented as proportions of patients with one or more transfusion with 95% confidence intervals (CI).
Results:
We identified 28,264 incident cancer patients, of whom 34.4% (95% CI: 33.9 –35.0) had received at least one RBC transfusion and 3.9% (95% CI: 3.7 – 4.2) at least one platelet transfusion within four months after diagnosis. A high proportion of patients who received any chemotherapy received RBC transfusions (57.9% (95% CI:56.4 – 59.5)) and platelet transfusions (16.1% (95% CI: 14.9 – 17.2)). The proportionof patients receiving transfusion varied by tumour site, with the highest use observed among cases of haematological malignancy (RBC, 63.7% (95% CI: 61.5 – 66.0);platelets 33.5% (95% CI: 31.3 – 35.7)). The proportion of patients receiving transfusions increased with higher tumour stage (e.g. of patients with stage I disease,25.9% (95% CI: 22.6 – 29.3) received RBC versus 47.5% (95% CI: 46.1 – 48.8) of patients with stage IV disease. For platelet transfusions these proportions were 2% (95% CI: 0.9 – 3.0) versus 5.6% (95% CI: 5.0 – 6.3).
Conclusion:
RBC and platelet transfusions are commonly administered among cancer-patients. Cancer treatment regimen, site and stage of disease are predictors for use of transfusions.

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EVIDENCE BASED MEDICINE: BLADDER CANCER

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In most Western countries, radical cystectomy is preferred over radiotherapy in treatment of muscle invasive stages of urinary bladder carcinoma and patients are only offered radiotherapy if they are unfit for surgery. A number of retrospective studies have shown that patients with urinary bladder cancer can be cured by radiotherapy. Local control rate after treatment is 60-70% and long term control is obtained in 40-50% of the patients. A large fraction of patients will have a systemic failure and dissemination at an early time point characterize the disease. 5-years survival rates are often 20-50%, between 24-50% when patients who are primarily selected for radiotherapy and 8-31% when radiotherapy is reserved for unfit patients. The volume to be treated in radiotherapy of bladder cancer remains unclear. Target volumes vary from partial bladder to the whole bladder including regional lymph nodes. It is often claimed that elderly people with bladder cancer do not tolerate radiation to a large volume including the lymph node. In contrast, others find that irradiation of elective lymph nodes followed by a boost to the bladder is tolerated with an acceptable level of toxicity. Pathology studies conclude that the risk of lymph node metastases is closely related to the T-stage and the lymph node at risk are the commen-, internal iliac- and upper external iliac nodes. Most often, radiotherapy to bladder cancer is given with 2 Gy per fraction to a total dose of 60 Gy. Increasing the dose with normo-fractionation has not improved the outcome and hypofractionation with biological high doses has not been proven beneficial. In a study on hyperfractionation, patients treated with a total dose of 84 Gy in 1 Gy fractions three times daily had better outcome compared to patients treated with a standard dose/fractionation schedule. However, this type of fractionation if only rarely used in treatment of bladder cancer. Bladder cancer is associated with a high risk of distant metastasis and neoadjuvant platin based chemotherapy have an effect on survival. Furthermore, a strategy including extensive transurethral resection of the bladder tumor combined with chemotherapy and radiotherapy has been introduced for the purpose of preserving the urinary bladder. In standard setting, an isotropic margin of 2 cm to account for day-to-day changes in target position is applied to the bladder. However, some studies have shown that an anisotropic margin may be more optimal. Focal boost to the macroscopic bladder tumor or the tumor bed after resection may be a way to improve the local control without increasing the probability of late reactions. IGRT combined with on board correction of tumor position may be a way to give a focussed high dose boost to the bladder tumor. In lymph node irradiation, IMRT may be superior to conventional 3- or 4-field techniques with sparing of the rectum and the bowel.

THERAPY PET-CT SCANNING - THE NURSING POINT OF VIEW

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The use of PET/CT scanning has dramatically increased over the last few years. PET/CT scanning with FDG is today an important imaging modality in diagnosing, staging, follow-up, localizing recurrence and for radiation therapy planning. By using the PET tracer FDG (fluordeoxyglucose) it is possible to define the metabolic activity of the tumour and with the CT scan to define the anatomical details and tissue homogeneities. With the combined PET/CT for therapy planning it is therefore possible to define the target volume and the risk organs, tailor the radiation treatment and hopefully reduce the side effects. The therapy PET/CT is especially valuable for head and neck cancer, esophageal- and cardia cancer, lung cancer, cervix cancer, anal cancer and lymphoma. From the patient's point of view the dual PET/CT imaging is more comfortable because just one scan session is necessary. Performing a therapy PET/CT scan is a complex session and demands trained staff. In our hospital we have a very successful collaboration with multidisciplinary teams from the PET department and the Radiotherapy department, both contributing with professional trained staff. Overall patient care is very important and a well-structured day for the planning session must be organized. The planning day includes a chain of different functions and communication flow, and the patient will meet a different person for each function, each an expert on their domain. The first step at arriving in the treatment unit is making an immobilization device and establishing a treatment chart. The patient will have a talk with one of the responsible nurses at the treatment unit, who informs the patient about the course of events for the treatment. The standard patient preparation for a PET/CT study is also used for a therapy PET/CT. To achieve optimal PET imaging data and to avoid artefacts and pitfalls, it is very important to follow the correct preparations, e.g. be fasting six hours before FDG injection, be well hydrated, avoid exercise and remember to keep warm, in order to avoid uptake in muscles and brown fat tissue. Patient positioning in the PET/CT scanner follows the same principles as for all therapy planning; comfortable for the patient, easily reproduced and secure. We use an external LAP-laser system for positioning and markings of the ISO-centre and reference points. The major subject when preparing and performing the therapy PET/CT scan is the radiation burden to the involved personnel. The FDG -tracer discharges photons with an energy of 511 keV and great penetrating ability. It is therefore important that all information handlings, moulding and other preparations have to be done before the tracer injection. The time with the injected patient should be minimised and the radiation burden should be shared between several personnel, who should be experienced and well trained in handling radioactivity.

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STEREOTACTIC BODY RADIOTHERAPY FOR MEDICALLY INOPERABLE STAGE I NON-SMALL CELL LUNG CANCER: MATURE OUTCOME AND TOXICITY RESULTS

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Purpose:
To report the mature outcome and toxicity results of stereotactic body radiotherapy (SBRT) in the treatment of medically inoperable patients with primary stage I NSCLC at the Aarhus University Hospital.
Materials:
Between 2000 and 2007, 89 consecutive patients were treated by linac-based SBRT using a body frame. Forty-five gray in three fractions (BED 112.5 Gy) over one week prescribed to the isocentre (67% isodose covering PTV) was given until 2004 when 67.5 Gy in 3 fractions (BED 219.4 Gy) was introduced for non-centrally located lesions. Forty-six percent of patients were under protocol while the remainder were retrospectively reviewed.
Results:
With a median follow-up of 44 months, 5 patients developed local failure. The local control rate at 4 years was 89% while the freedom-fromfailure was 36%. The 2-,3- and 5-year cancer specific survival was 72%, 64% and 50% respectively, with a median of 61 months. The median overall survival was 22 months. No significant differences in control or survival rates were observed between dose schedules. Seventy-eight percent of all worst toxicity grade scores were grade 0 or represented no change from baseline. Of all toxicities above baseline, the most frequent was asymptomatic pulmonary fibrosis (20.4%), followed by worsening of performance status (14%) and dyspnea (11.7%). Most toxicity was grade 1 (67.9%) with 14% grade 3/4. This profile was consistent during both the acute/subacute and late onset periods, with the exception of the most frequent toxicity: asymptomatic pneumonitis dominated the subacute period progressing to fibrosis in the late period. No significant difference in the toxicity profiles was observed between dose schedules.
Conclusions:
Longer follow-up confirms the excellent local control and encouraging survival outcomes of SBRT for inoperable early stage NSCLC. The late toxicity is characterized by radiographic changes and decline in lung function/ PS. No significant gain in control with a BED > 112.5 Gy was observed and therefore use of a lower dose/fraction schedule for centrally located lesions is recommended. SBRT is now the standard of care for inoperable stage I NSCLC at Aarhus University Hospital. A Scandinavian randomized trial is presently recruiting to formally compare SBRT with conventionally fractionated radiotherapy.

CAN RESPIRATORY COACHING FOR 4D CT EMULATE FREE BREATHING DURING THE TREATMENT COURSE?

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Purpose:
Using 4D CT and finding the midventilation scan for planning in lung cancer radiotherapy diminishes the risk of introducing a systematic error caused by tumor motion. The image quality of 4D CT depends on breathing regularity. Respiratory coaching may improve regularity, facilitating less motion artifacts. We question the safety of coached planning 4D CT without coaching during treatment. For this purpose we investigated whether it is possible to coach to a more regular breathing close to the free breathing.
Materials:
Eleven volunteers, recruited among health professionals in the department, went through auditive respiratory coaching on three different days within a two week period. The RPM system (Varian) was used to track the respiratory motion. On all days, free breathing and two coaching modes were recorded. All breathing curves are being analyzed regarding amplitude to find inter- and intrasession variations. We assumed that first day's free breathing simulated an uncoached 4D CT planning and compared the mean amplitude to the mean amplitudes of the free and coached breathing from day two and three. We equally assumed that the coached breathing from day1 simulated a coached 4D CT planning and compared the mean amplitude to the mean amplitudes from the free and coached breathing from day two and three (two tailed T-test, $p<0.05$).
Results:
Comparing the first day's free breathing with free breathing the following days revealed a significant increase in amplitude for seven volunteers and a significant decrease for two. Comparing the first day's coached breathing to free breathing the following days showed an increase in amplitude for half the volunteers and a significant decrease for two. Comparing first day's coached breathing to the coached breathing the following days showed a significant increase in amplitude for nine volunteers and a significant decrease for two.
Conclusions:
These preliminary results suggest that large interfraction variation is present in breathing amplitude irrespective of coaching. This suggests that daily image guidance should be applied to verify respiratory pattern and tumor related motion. Fluoroscopy studys investigating the effect of coaching on the interfraction tumor motion is warranted. Until further investigated it is not recommendable to use coached 4DCT for planning of a free breathing treatment course.

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CLINICAL CASE: BREAST - FOCUS ON THE BENEFIT OF GATED DELIVERY IN INSPIRATION OR DEEP INSPIRATION

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Breast radiotherapy has evolved over the past century to provide the most contemporary technique using a non-divergent co-planar tangential field beam. Such technique is challenged with the geometry of often large breast size or internal mammary lymph node co-irradiation with mediolateral target extensions bending concavely around risk organs, and with respiratory motion of target and risk organs, and with fluctuation of lung tissue density. In the adjuvant setting the majority of patients are over treated, but all are at risk of cardiopulmonary side-effects This concern regards particularly heart and coronary arteries in left-sided cases, potentially offsetting the survival benefit, thus emphasizing the need for further reduction of the low risk of cardiac side effects. The aim of respiratory gating in breast radiotherapy is to implement a comprehensible technique applicable to a large patient group, and to reduce radiation doses to risk organs, without compromising doses to target structures. Inspiration implies posteroinferior displacement of the heart, consistently indicating that only a slight change in heart position appreciably impacts the volume in field of left-sided cases. Furthermore, lung inflation significantly reduces volume of lung in the high dose region irrespective of side. In contrast to intensity modulation, no change in target or contralateral organ doses are experienced. Free breathing gating compares well with deep inspiration breath-hold in terms of dosimetric risk organ sparing. Breast patients show good breathing compliance, why audio coached enhanced free breathing gating further improves the spatial organ separation and thereby favourises the dosimetric benefits for breast conservation as well as mastectomy cases. For routine gated patients the calculated normal tissue complication probabilities compare well with the predicted values from pre-clinical computer tomography studies. At Rigshospitalet, Denmark, gated breast radiotherapy has been in routine use since 2004 as standard of care for left-sided cases requiring internal mammary lymph node co-irradiation, with more than 350 patients treated so far. Less than 10% of patients eligible are excluded from this technique, primarily due to non-compliance. Except from individualised patient respiration training, treatment planning as well as slot times are resource equal to non-gated treatments.

IMRT for breast cancer: a new standard?
WHEN TO CONSIDER IMRT FOR BREAST CANCER?

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Breast irradiation takes up approximately half of the numbers of patients treated in our department of radiotherapy, calling for standard methods or class solutions. Five years ago, most centres used 2D treatment planning for breast cancer radiotherapy, but today the question is if IMRT should be the standard planning method. Numerous publications have evaluated the potentials of IMRT suggesting improved dose homogeneity, reduced toxicity and efficacy, although not all patients will benefit from IMRT. We only use IMRT as our standard for very few patients. The three main reasons for this are; IMRT is associated with large patient volumes receiving a low dose, it is not possible to predict which patients will gain form IMRT, and IMRT is more sensitive to target motion than conventional 3D CRT. Radiotherapy for breast cancer is complicated with a challenging target geometry that bends concavely around the organs at risk. The long term toxicity of the treatment includes excess mortality which is important for this group of patients who are most likely to be cured. This challenge calls for optimal target coverage and precise evaluation and minimisation of dose to organs at risk. We use to the national guidelines from the Danish Breast Cancer Cooperative Group for target definition and dose constrains to organs at risk. With respect to these guidelines most patients can be treated with conventional 3D CRT. For patients with stage II left sided breast cancer (both lumpectomy and mastectomy), we include parasternal node irradiation. In these cases we have used gating with audio coaching as the standard treatment since 2004 to minimise dose to organs at risk. 3D CRT and the use of gating for the mentioned left sided cases, together with careful evaluation of the target definition, produce sufficient plans for 99% of our breast cancer treatments. For the remaining patients we have used IMRT. In all we have treated 29 breast cancer patients, of more than 900 patients treated with IMRT the last 7 years at Rigshospitalet. For more than 60% of the breast cases, IMRT was combined with gating and 8 patients had bilateral cancer. The experiences we gained from gating, controlling the extend of the respiratory motion, and the on-line and off-line verification and correction of this motion, have been valuable introducing IMRT. With IMRT we want to keep the respiratory motion of the target as low as possible, to rely on the calculated dose distribution. We use vacuum bags to immobilise the patient and this immobilisation reduces the anterior posterior motion of the breast during breathing with 50% compared to patients without immobilisation. The spontaneous anterior posterior breathing motion is reduced to a mean value of 2.5 mm after immobilisation. Knowing the motion to be minimal in one direction, it is possible to optimise the beam configuration and the leaf motion accordingly.

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IMPROVED SURVIVAL AND RESPONSE TO RADIOTHERAPY IN HPV-RELATED OROPHARYNGEAL CARCINOMAS - A SUBGROUP ANALYSIS OF THE RANDOMIZED DAHANCA 5 & 7 TRIALS

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Purpose:
Expression of p16 is highly correlated to infection with HPV in oropharyngeal carcinomas. The aim of this study was to evaluate the impact of p16 expression on treatment response and survival in a prospectively analyzed cohort of Danish oropharyngeal cancer patients treated with radiotherapy according to the randomized DAHANCA 5 & 7 trials.
Materials:
Between January 1986 and December 1999 The Danish Head and Neck Cancer group (DAHANCA) conducted the nationwide DAHANCA 5 & 7 randomized trials, focusing on overcoming the disadvantages of tumour cell hypoxia and accelerated tumour cell proliferation in relation to radiotherapy. (Overgaard J. et al. Radiother. Oncol. 46; 1998:135-146. Lancet 2003; 362: 933-940). In the present study, 335 oropharyngeal tumour tissues from patients enrolled in these trials were evaluated by immunohistochemistry for p16 expression. Tumours were classified as p16 positive in case of a strong, confluent nuclear and cytoplasmatic staining pattern or p16 negative (absence of staining).
Results:
In total, 135 of the 335 oropharyngeal tumours were p16 positive corresponding to 40%. No statistical significant differences were observed between the p16 positive and p16 negative groups regarding tumour stage, gender, and age. Loco-regional tumour control was significantly improved for p16 positive tumours compared to p16 negative, with 5-year actuarial values of 67% versus 36% ($p < 0.0001$). A similar beneficial outcome for p16 positive tumours was observed for the 5-year actuarial values for cancer specific survival (69% versus 35%, $p < 0.0001$) and overall survival (54% versus 18%, $p < 0.0001$). In a Cox proportional hazard multivariate analysis p16 expression remained a very strong independent prognostic factor for loco-regional tumour control [OR: 0.34 (95% C.I. 0.23 - 0.50)], cancer specific death [OR: 0.28 (0.19 - 0.42)] and overall death [OR: 0.32 (0.23 - 0.45)]. p16 was an even stronger prognostic factor related to these outcomes than the clinical parameters T-stage and Nodal-status.
Conclusions:
Expression of p16 is significantly correlated to improved survival and loco-regional tumour control in oropharyngeal cancer patients treated with radiotherapy. p16 status proved to be the strongest independent prognostic factor altogether and as such it has been implemented as a prerandomization stratum in ongoing and future clinical trials initiated by DAHANCA. Presented on behalf of the Danish Head and Neck Cancer group (DAHANCA)

CAN RESPIRATORY COACHING FOR 4D CT EMULATE FREE BREATHING DURING THE TREATMENT COURSE?

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Purpose:
Using 4D CT and finding the midventilation scan for planning in lung cancer radiotherapy diminishes the risk of introducing a systematic error caused by tumor motion. The image quality of 4D CT depends on breathing regularity. Respiratory coaching may improve regularity, facilitating less motion artifacts. We question the safety of coached planning 4D CT without coaching during treatment. For this purpose we investigated whether it is possible to coach to a more regular breathing close to the free breathing.
Materials:
Eleven volunteers, recruited among health professionals in the department, went through auditive respiratory coaching on three different days within a two week period. The RPM system (Varian) was used to track the respiratory motion. On all days, free breathing and two coaching modes were recorded. All breathing curves are being analyzed regarding amplitude to find inter- and intrasession variations. We assumed that first day's free breathing simulated an uncoached 4D CT planning and compared the mean amplitude to the mean amplitudes of the free and coached breathing from day two and three. We equally assumed that the coached breathing from day1 simulated a coached 4D CT planning and compared the mean amplitude to the mean amplitudes from the free and coached breathing from day two and three (two tailed T-test, $p<0.05$).
Results:
Comparing the first day's free breathing with free breathing the following days revealed a significant increase in amplitude for seven volunteers and a significant decrease for two. Comparing the first day's coached breathing to free breathing the following days showed an increase in amplitude for half the volunteers and a significant decrease for two. Comparing first day's coached breathing to the coached breathing the following days showed a significant increase in amplitude for nine volunteers and a significant decrease for two.
Conclusions:
These preliminary results suggest that large interfraction variation is present in breathing amplitude irrespective of coaching. This suggests that daily image guidance should be applied to verify respiratory pattern and tumor related motion. Fluoroscopy studys investigating the effect of coaching on the interfraction tumor motion is warranted. Until further investigated it is not recommendable to use coached 4DCT for planning of a free breathing treatment course.

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CHARACTERIZATION OF SQUAMOUS CELL CARCINOMAS OF THE SUPRAGLOTTIC LARYNX WITH OR WITHOUT MUTATIONS IN TP53

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Purpose:
Objective: Tobacco smoking is the primary etiology for squamous cell carcinomas of the supraglottic larynx and is reported to initiate the carcinogenic process by inducing mutations in TP53. However, not all supraglottic larynx carcinomas have mutations in TP53 and a distinct molecular profile might separate tumors with or without TP53-mutations. The aim of the present study was to characterize possible differences in key-proteins in supraglottic larynx tumors according to the TP53-mutational status.
Materials:
Paraffin-embedded formalin fixed pretreatment biopsies of 123 patients with squamous cell carcinomas of the supraglottic larynx was collected from patients treated with radiotherapy with curative intent between January 1986 and December 1999 according to the DAHANCAguidelines: 66-68 Gy, 2 Gy/fx, 5-6 fractions/week and concomitant radiosensitizer (nimorazole). For estimation of TP53-mutations, DNA was extracted from the biopsies and screened for mutations in exon 4c-10 of TP53 by DHPLC (WAWER). Mutations were further characterized by sequencing. EGFr, p16, KI-67, BCL2 and E-cadherin were estimated by immunohistochemistry. Data were evaluated by descriptive statistics, Spearman's test for trend and logistic regression analysis.
Results:
62 carcinomas were wildtype or had silent mutations out side the domains, 61 had mutations inside the domains or null-mutations leading to stop-codons. The TP53-mutational status was not correlated to the expression of E-cadherin, BCL2 and KI-67 or tumor cell differentiation. High expression of EGFr seemed to be correlated to tumors with mutations in TP53 (p=0.03) and TP53 wildtype tumors had twice as high expression of p16 compared to carcinomas with mutations in TP53 (p=0.04). Furthermore, logistic regression analysis separating by mutational status, suggested that carcinomas with mutations in TP53 had relative higher expression of EGFr (p=0.03, RR=2.6 (1.1-6.3)) and lower expression of p16 (p=0.04; RR=0.4 (0.2-0.9)) compared to wildtype tumors or tumors with silent mutations outside the domains.
Conclusions:
The results of the present study suggest that low expression of EGFr and high expression p16 might be two of the markers that characterize tumors without mutations in TP53. These data are in accordance with experimental data and indicate that other factors than tobacco (i.e. HPV-virus) might be involved in the carcinogenic process of squamous cell carcinomas of the supraglottic larynx.

Cancer epidemiology
THE CHANGING PICTURE OF CANCER IN EUROPE

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It was estimated that 3 191 600 new cancer cases (excluding non-melanoma skin cancer) and 1 703 000 cancer deaths occurred in 2006 in Europe of which 53% and 56% respectively occurred in men. The increase in 2 years was estimated to be 300 000 cases. The ageing of the European population alone will increase these numbers in the future and cancer will continue to be a major public health problem. The most common cancer was breast cancer followed by colorectal and lung whereas the mortality was highest for lung followed by colorectal, breast and stomach cancer. The cancer picture is however changing, both with respect to incidence, mortality and survival and the differences between the European countries with the respect to these variables are under intense surveillance and study. This has lead to the development and interest in national cancer control plans although none so far has been developed for EU. The need for better and comparable data is obvious, and clearly demonstrated in the collaboration by the Nordic countries on incidence, mortality, prevalence, survival, and predictions for the future. The presentation will be based on recent European and Nordic publications and available databases and software that can demonstrate the changing picture of cancer in Europe and point to plausible reasons behind the observed changes. Better access to care, early diagnosis and better treatment will influence mortality, survival and prevalence whereas prevention like actions to curb the tobacco epidemic will reduce the incidence of several cancers and other important exposures may led to incidence increase on top of the increase caused by ageing

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QUALITY ASPECTS OF IGRT EUROPEAN INSTITUTE OF RADIOTHERAPY 1ST TASK GROUP REPORT, AND SOME GENERAL ASPECTS OF IGRT QA

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Background:
In mid-2007, the first task group under the auspices of the European Institute of Radiotherapy (EIR) was formed to provide a review of the current status of 3D CT-based image guided in-room systems and their pertinent application for image guidance. This addresses both technical and practical issues, and an approximate estimation of work practices including work flow issues.
Material and Methods:
The systems of four major vendors of CT-based in-room image guidance systems have been specifically evaluated; Elekta, Siemens, Tomotherapy and Varian solutions, together with the generic workflow processes for system implementation, capabilities and use. Workflow evaluation has been performed by sending out a questionnaire to a number of clinics in Europe. The clinics were asked to report timing (and comments) for processes including image acquisition, reconstruction, analysis and application of corrections for prostate and head&neck cancer cases.
Results:
The task group has produced the report "3D CT-based in-room image guidance systems: a practical and technical guide" relaying the outcome of the group's work within the subject. The report consists of sections covering generic issues of MV and kV CT-based techniques, technical specifications of several image guidance systems, as well as user provided information on the clinical workflow for the selected user cases.
Conclusions:
This report proposes and aims to provide a common platform for assessment of the properties of the different systems and their clinical implementation, with respect to both technical and workflow issues. This report also provides a check list with suggestions for aspects to consider when purchasing 3D CT-based image guidance systems, as well as for the handling of your chosen system.

STEREOTACTIC BODY RADIOTHERAPY FOR MEDICALLY INOPERABLE PATIENTS WITH STAGE I NON-SMALL CELL LUNG CANCER. AN EARLY REPORT FROM A PROSPECTIVE PHASE II STUDY

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Within the Nordic study group of Stereotactic Body Radiotherapy (SBRT) we have previously shown an 88% local control with a median dose of 15 Gy x 3 in medically inoperable patients with stage I non small cell lung cancer (NSCLC). From a prospective phase II study on the same patient category we now report on local control, survival and toxicity as related to severity of COPD and cardio vascular disease CVD.Sixty patients from Sweden, Norway and Denmark entered the study from Aug. 2003 to Sept. 2005. Fiftyseven patients with T1 (65%) and T2 (35%) and a median age of 75 years (range 59-87 y) were evaluable. At baseline mean FEV1% was 64% and mean Karnofsky index was 80. The patients were further subdivided in four groups according to severity of COPD (GOLD criteria). SBRT was delivered in the Stereotactic Body Frame (SBF) with 15 Gy x 3 to the 67% isodose of the periphery of the PTV.At a median follow-up of 24 months the local control rate was 96%. Nine patients (16%) had local failure, regional- or distant metastases. Twenty patients (35%) died during follow-up and in 20% (4/20) of the cases death was related to lung cancer. The 1- and 2-years overall survival was 86% and 65% respectively. No grade 4 or 5 toxicity was reported. Grade 3 toxicity was seen in 12 patients (21%). There was no significant decline of FEV1% during follow up independent of GOLD status. No decrease in performance status could be seen in the whole patient group but the CVD group had a significantly larger decrease than the COPD group. Final survival and response data will be presented at the time of the meeting.SBRT for stage I NSCLC results in a favourable local control rate with acceptable toxicity, even for the patients with highly impaired medical condition due to COPD.

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INTERSTITIAL PDR BRACHYTHERAPY MAY COMPENSATE AN R1 RESECTION IN ADVANCED RECTO-SIGMOID CANCER

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Purpose:
To evaluate outcome of extensive abdomino-pelvic surgery combined with interstitial pulsed dose rate (PDR) brachytherapy (BT) in locally inoperable primary or recurrent recto-sigmoid cancer.
Materials:
45 patients with rectal (41) and sigmoid cancer (4) referred from all parts of Denmark and consecutively operated 2001-2007 were evaluated. There were 18 primaries and 27 recurrent cases. Median age was 60 years (38-81). Patients were selected for this very extensive treatment when R0 resection close to muscle and bone in the posterior pelvis was considered impossible based on preoperative pelvic MR and palpation in general anaesthesia. Patients were screened for disseminated disease by CT and US or PET-CT. Thirty-three patients not previously irradiated were given preoperative long course chemo-radiotherapy (46-60 Gy/25-30 fx). Following resection of tumor and all involved pelvic organs the BT catheters were sutured in parallel at a distance of 1-1.5 cm and the tumor bed was marked with silver clips. A vertical rectus abdominis myocutaneous (VRAM) flap was used to cover the BT catheters and reconstruct the perineal defect. Guided by the preoperative MRI and the silver clips the target for PDR BT was contoured at 5 mm distance from the catheters. The average target volume was 33 cm3. Prescribed PDR dose at 0.5 mm from the catheters was 25-30 Gy, 0.5-0.6 Gy/pulse, 1 pulse/hr. BT was initiated between 1-7 days after the operation. Postoperative radiotherapy (25 Gy/15 fx) to the tumor bed only were used in patients irradiated for previous disease in the pelvis.
Results:
R0 resection was obtained in 16, R1 in 27 and R2 resection in 2 patients, respectively. Bricker bladder was used in 25 and all patients received a colostomy. A median of 4.5 (3-8) BT catheters were used to cover the tumor bed. The 30 day mortality was 0%. However, one patient did not recover and died from septicaemia at day 64. Late toxicity comprised moderate neuropathy in 6, fistula in 5, subileus in 3, soft-tissue necrosis in 2, hydronephrosis in 2, insufficiency fracture in 1 and ureter leakage in 1 patient. Three year overall-survival (OS±SE) was 62%±8, local control (LC±SE) 66%±9 and disease free survival (DFS±SE) 38%±8. The number of BT catheters (3-4 vs. 5-8) significantly ($p<0.03$) influenced LC (79% vs. 49%) and DFS (57% vs. 18%). In contrast, the status of the resection margin (R0 vs. R1) did not influence LC (66% vs. 71%) and DFS (42% vs. 38%).
Conclusions:
Meaningful disease control and survival can be obtained in selected patients with locally advanced inoperable primary and recurrent rectosigmoid cancer by employing extensive surgery and PDR BT. The data suggest that PDR BT may compensate for a close or involved surgical margin limited to a tumor bed with an area of approximately 50 mm in maximal diameter.

INTRAPERITONEAL ALPHA-RADIOIMMUNOTHERAPY OF OVARIAN CANCER - PHARMACOKINETICS AND DOSIMETRY OF 211-ATMX35 F(AB')2 IN A PHASE I STUDY

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Purpose:
The alpha particle-emitter 211At labeled to a monoclonal antibody has in several animal studies proved effective in treatment of microscopic ovarian cancer in the peritoneal cavity. In this study pharmacokinetics and radiotoxicity are evaluated in patients after intraperitoneal injection of 211At- MX35 F(ab')2.
Materials:
Nine patients in good remission following second-line chemotherapy for recurrent ovarian carcinoma participated in the study with informed consent. The patients underwent laparoscopy and peritoneal scintigraphy before the therapy. During the laparoscopy a peritoneal catheter was inserted and the peritoneal cavity was inspected to exclude presence of macroscopic tumor growth or major adhesions. The scintigraphy was made to study the fluid distribution in the peritoneal cavity. For the therapy, patients were infused with 33-172 MBq 211At-MX35 F(ab')2 in 1-2 L Extraneal solution via the peritoneal catheter. The remaining solution was drained from the peritoneal cavity after 24h. Gamma camera whole body scans were made at 1, 6, 12 and 24h. All urine and samples of blood and peritoneal fluid were collected at 1 48h and measured for radioactivity content.
Results:
The 24h and 48h urinary excretion of 211At was 2% and 8% respectively. The thyroid uptake was 1% at 24h in the first five patients. The following patients were effectively blocked by potassium perchlorate. No other organ uptake could be detected. Estimated absorbed radiation doses were: to bone marrow 0.08 mGy/MBq, to unblocked thyroid 15 mGy/MBq and to the peritoneal surface 8 mGy/MBq. No adverse effects were observed in laboratory parameters or subjectively.
Conclusions:
At least 150 MBq of 211At-MX35 F(ab')2 in 1-2L solution could safely be administered intraperitoneally. Extrapolation from animal data indicates that this activity level should result in sufficiently high absorbed doses to erradicate micrometastases on the peritoneum.

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OUTCOME OF LARGE V20 IN THE RADIOTHERAPY OF NSCLC

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Purpose:
High radiation dose to the lungs is associated with a worse outcome after radiotherapy (RT). The V20 the percentage of the lunge receiving a specific dose is used as a measure of the exposure of the lung to radiation. From 1995 to 2006 356 patients with non-small cell lung cancer received 3-D conformal RT with doses exciding 60 Gy in 30 fractions. According to the radiation protocols used a V20 up to 50% were allowed, and 79 patients (22%) had V20_40%. We have retrospectively analysed the outcome of these patients.
Materials:
The patients were prospectively registered for RT dose, dose distribution to the lungs and the tumour, vital status and causes of death. Measurements of FEV1 and FVC were obtained for each follow-up. Information of side effects was retrospectively obtained from the patient files.
Results:
As of Feb. 2008 303 patients were dead, 247 due to lung cancer, 14 of infection or treatment toxicity, and 42 due to courses not related to the cancer. In a univariate analysis the patients receiving V20 _40% had significant reduced survival compared with he patients receiving less the 3-year survival being 6% and 31%, respectively. The number of death due to infection or treatment toxicity did not differ between the groups. In a Cox analysis it was still a statistical significant factor together with performance status (PS), GTV, and gender while age, FEV1 at start of RT, stage and history of smoking were not of significance. If the analyses were restricted to death not due to the cancer, PS, GTV, and V20 _40% were significant factors, but V20 _40% and GTV were still significant factors with PS being of borderline significance. If the analyses were restricted to patients surviving 2 years, the V20_40% were still a significant factor for death and cancer death, but not death of other reasons. In logistic regression analyses the V20 together with poor pre-treatment FEV1 predicted occurrence of dyspnoe grade 3 during the first 3 months after radiation while other parameters were of no significance. V20_40% did not influence a decrement in FEV1 and FVC obtained 3, 6, 12, 24, 36, or 48 months after start of RT compared with the pre-treatment values.
Conclusions:
Large V20 is associated with poor survival but the excess death rate was caused by the cancer not toxicity. Large V20 was associated with occurrence of dyspnoe during the first 3 months, but did not influence measurement of FEV1 and FVC.

ABDOMINAL RESPIRATORY MOVEMENT FOR PANCREATIC CANCER PATIENTS

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Purpose:
The uncertainty in tumour position in the transition from CT scan to the actual treatment can be divided into preparation errors (systematic errors) and treatment execution errors (random errors). A standard CT scan can capture the tumour in an extreme position which introduces a large systematic error and therefore large margins are required to compensate for this. This problem can be solved by CT scans that are a function not only of the spatial coordinates but also of the respiration phase (4D-CT). The purpose of this study has been, based on 4D-CT, to determine the standard deviation and peak-to-peak amplitude of the respiratory movement of pancreas and kidney and also to determine the standard deviation of the distribution of tumour positions in the mid-ventilation phase (the phase closest to the mean tumour position) relative to the mid-ventilation point (the mean tumour position).
Materials:
In total 40 patients assigned to radiotherapy of inoperable pancreatic cancer from Nov. 2006 to Feb. 2008 were 4D-CT scanned. The kidneys and pancreas were delineated and subsequently automatically tracked in 3D by rigid registration and their registration parameters were analysed with respect to organ motion in the three spatial coordinates.
Results:
More than 100 organs were tracked in 40 4D-CT scans. The average peak-to-peak amplitudes of the abdominal organ motion were measured and the standard deviations (SD) of the movement distributions were calculated in all three spatial coordinates. The averaged peak-to-peak motion for the pancreas and the kidneys in the Left-Right (LR) and Anterior-Posterior (AP) directions were of the order of 2 mm. The CC movement for the pancreas was 8.0 mm, which was smaller than the detected average kidney movements of 11.4 mm. The standard deviations of the respiration movement of the pancreas were in the three directions: LR: 0.8 mm, AP: 0.9 mm and CC: 3.4 mm (1 SD). For the Left/Right kidney the corresponding figures were: LR: 1.2 mm/0.7 mm, AP: 1.1 mm/1.3 mm and CC: 4.6 mm/4.7 mm. The residual errors (standard deviation of the distribution of tumour positions in the mid-ventilation phase relative to the mid-ventilation point) were for the pancreas: LR: 0.4 mm, AP: 0.4 mm and CC: 0.8 mm (1 SD). For the left/Right kidney the residual errors were: LR: 0.7 mm/0.4 mm, AP: 0.4 mm/0.5 mm and CC: 1.0 mm/1.2 mm (1 SD).
Conclusions:
From on the determined standard deviations of the respiration movement of the pancreas it has been possible to reduce the margins utilized at our institution for ordinary 3D CT - the movement is less than we previously expected. This has led to a decrease in PTV volume of 34%. Furthermore, it is possible for this patient group to reduce the volume of the PTV by an additional 22 % by selecting the mid-ventilation phase of the 4D-CT scan compared to a conventional 3D-CT scan.

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INTER- AND INTRAFRACTIONAL MOVEMENT OF THE TUMOUR IN EXTRACRANIAL STEREOTACTIC RADIOTHERAPY OF NSCLC

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Purpose:
The purpose of this study is to determinate the appropriate treatment planning margins related to inter- and intra-fractional respiration induced movements as well as setup accuracy in a stereotactic body frame for stereotactic treatments of NSCLC patients.
Materials:
From August 2005 to January 2008, 17 patients with NSCLC where given a stereotactic treatment. The patients were scanned with normal and uncoached respiration without use of abdominal compression. Each patient had CT-scans performed at four occasions throughout the treatment: As part of the CT-simulation and before the 3 radiotherapy treatment. At every occasion six individual CT-scans covering the tumour volume were obtained. In this way 24 scans where obtained from each patient. In each CT-scan the maximum positions of the tumour where located in all 6 directions, represented by the top, bottom, anterior, posterior, left and right part of the tumour. These coordinate constitute the data of this study. A common reference system between the individual CT sessions is obtained by fusion of the patient anatomy of a given CT session with the patient anatomy of the first CT session. Likewise a fusion of the body frame was performed to be able to measured patient positioning accuracy within the frame. All fusions were performed in the Syntegra module in the Pinnacle3 dose planning system.
Results:
The standard deviations of the respiration induced intra-fractional movements were: LR: 0.8 mm, AP: 1.2 mm and CC: 2.2 mm (1 SD). The inter-fractional movements were: LR: 1.0 mm, AP: 1.3 mm and CC: 1.9 mm (1 SD). Finally the set up accuracies in the body frame were LR: 1.5 mm, AP: 1.1 mm and CC: 1.8 mm (1 SD). The standard deviation of all three uncertainties would be LR: 2.0 mm, AP: 2.1 mm and CC: 3.4 mm (1 SD)
Conclusions:
With a patient fixated in a stereotactic body frame, we conclude that large movements of the tumour are rarely seen within the lung. With consecutive scans, using a conventional CT-scanner, it is possible to find those patients in whom the tumour movement is large. The three discussed uncertainties would by use of the van Herk (IJROBP pp. 11211135, 2000) margin recipe be 10.2 mm in the CC direction. Three possible way of reducing this margin could be 1) use of mid-ventilation phase (4D CT) for treatment planning 2) use of Cone Beam treatment position verification (registration of tumour not bone) 3) use of gating. Simple estimates of the effect of these changes is that 4D CT could reduce the margin to 8.6 mm. Cone Beam in combination with 4D CT would reduce the margin to 5.2 mm. However addition of gating would at most reduce the margin with one millimetre. Thus in our opinion gating is only useful for a very limited number of patient with substantial tumour movements. However, introduction of 4D CT and Cone beam verification is strongly encouraged

SETUP ERRORS IN PATIENTS WITH HEAD-AND-NECK OR LUNG CANCER TREATED WITH IMAGE GUIDED RADIOTHERAPY ARE NOT CORRELATED WITH WEIGHT, HEIGHT, BMI, OR WEIGHT LOSS

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Purpose:
The purpose of this study was to quantify the setup errors of patient positioning during IGRT and to correlate setup errors to patient-specific factors such as weight, height, BMI, and weight loss.
Materials:
34 consecutively treated head-and-neck cancer patients (H&N) and 20 lung cancer patients were investigated. Patients were positioned using customized immobilization devices consisting of a vacuum cushion with a full thermoplastic face mask for H&N while lung cancer patients were immobilized with arms up in a thermoplastic shell from the chin to the umbilicus. Treatment was given in supine position on an Elekta Synergy accelerator. Cone beam acquisitions were obtained according to a standardized Action Limit protocol and compared to pre-treatment CT images. Patient position at treatment was assessed using an automatic grey scale matching algorithm in a predefined volume (clip box) according to set-up protocols for H&N and lung. The average 3D deviation from three initial cone beam scans was compared to deviations at the 10th and 20th treatment session and correlated by linear regression analysis to height, weight, and BMI, and in H&N to weight loss as expressed by the relative weight change over time.
Results:
The SD of the translational and rotational setup errors during the first three sessions were 0.9 mm (Left-Right), 1.1 mm (Anterior-Posterior), 0.7 mm (Cranio-Caudal) and 0.7 (LR-axis), 0.5 (AP-axis), and 0.7 (CC-axis) for H&N. The equivalent data for lung cancer patients were 1.1 mm (LR), 1.1 mm (AP), 1.5 mm (CC) and 0.5 (LR-axis), 0.6 (AP-axis), and 0.4 (CC-axis). The median BMI for H&N and lung at the beginning of treatment was 25.8 (17.6-39.7) and 23.7 (17.4-38.8), respectively. Overweight (BMI>25) was observed in 46% (25/54). The median weekly weight change for H&N was -0.3% (-2.0% to 1.1%). With H&N and lung cancer analyzed separately, no statistically significant correlation was observed between setup errors and height, weight, BMI, or weight change during treatment, irrespectively whether the 3D deviations from the initial three cone beam scans or scans from the 10th or 20th treatment session were used.
Conclusions:
No correlation was observed between the magnitude of setup errors during IGRT and patient-related factors such as height, weight, BMI, and weight loss. The present immobilization has ensured a safe positioning during radiotherapy despite weight loss and a large proportion of overweight patients.

Vidste du at...?

... der er et nyt sundhedscenter på vej i Københavns Kommune.
I foråret 2007 åbnede Sundhedscenter for Kræftramte i Ryesgade med plads til at hjælpe ca. 400 patienter om året. På grund af pladsmangel har tilbuddet om rehabilitering kun omfattet patienter med tre kræftsygdomme: bryst-, lunge- eller tarmkræft, men nu har Københavns Kommune bevilget 45 mio. kr. til at opføre et helt nyt sundhedscenter på hjørnet af Tagensvej og Nørre Allé, som skal have kapacitet til at hjælpe 1.000 kræftpatienter årligt uanset diagnose. Centret ventes færdigt i 2010.

Kilde: Berlingske Tidende, 24. sept. 08

... Yondelis® (trabectedin) er aktiv ved ovariecancer.
Ved ESMO konferencen i Stockholm i september 2008 præsenterede Prof. Bradley Monk, University of California Irvine Medical Center, resultaterne fra en randomiseret undersøgelse med 672 patienter med ovariecancer, som progrediered-de på 1.linie behandling. Yondelis plus pegyleret liposomal doxorubicin (Doxil®Caelyx®) blev sammenlignet med Doxil® alene. Progressionfri overlevelse (PFS) var hhv. 7,3 og 5,8 måneder (p=0.019) og response rate 28% vs. 19%. Overlevelses-data forventes inden for de næste 12 måneder.

Prof. Bradley Monk, Presidential Symposium, ESMO Congress Stockholm 2008

... radioterapi kan øge risikoen for at udvikle kolon- og rektumcancer efter behandling for prostatacancer.
I et studie, der inkluderede 1,134 patienter med prostatacancer diagnosticeret mellem 1980 og 1998 og med en overlevelse på mindst 5 år blev 264 patienter behandlet med extern radioterapi. Patienterne blev fulgt indtil slutningen af 2003, hvor ialt 19 patienter havde udviklet kolorektal cancer. Sammenlignet med den almindelige befolkning var risikoen for at udvikle koloncancer signifikant forhøjet, mens rektalcancer ikke viste højere incidence. Risikoen for kolon-cancer var forøget i perioden 5-9 år efter diagnosen. Patienter, der ikke var blevet behandlet med stråleterapi, havde ingen forøget risiko for rektal eller kolon cancer.

Epidemiology, Intl J Cancer
123;5:1141-5

... kun de færreste af de registrerede kliniske forsøg, der omhandler kræftbehandling, bliver publiceret.
Siden efteråret 1999 har investigatorer været forpligtet til at registrere alle kliniske forsøg hos National Institute of Health (NIH). I alt 44232 forsøg er registeret i perioden 1999-2007, af hvilke 11829 er cancer-relateret, og blandt disse identifice-rede forfatterne 2028 som omhandlede behandling af kræftsygdomme. Af disse fandtes 17.6% af være publiceret iflg. PubMed. Kliniske undersøgelser sponsoreret af de kooperative grupper og NIH havde publikationsrater på 59% vs 5.9% for undersøgelser sponsoreret af industrien. Blandt de publicerede undersøgelser bragte 64.5% positive resultater.

Ramsey S, Scoggins J
The Oncologist 2008;13:925-9.

SKA's kursusprogram - forår 2009

Tilmelding - *gældende for alle nedenstående kurser:*

Tilmeldningsblanken hentes på *www.skaccd.org* og faxes til SKAs sekretariat, fax: 3535 6906 eller e-mail: june.thygesen@rh.regionh.dk eller evt. post: Rigshospitalet, June Thygesen SKA, 5072, Blegdamsvej 9, 2100 Kbh. Ø

SKA sekretærkursus: "Kræftsygdom og -behandling" - Modul I

Dette populære kursus afholdes nu for 4. gang. På Modul I kurset gennemgås de mest almindelige kræftsygdomme, den eksperimentelle behandling, fase 1-3 protokoller samt sekretærens mange samarbejdsrelationer, udfordringer - og muligheder.

Kursusleder: Sekretær June Kayser Thygesen
Tid og sted: 14. januar 2009
Hotel Kong Arthur, København
Kursusafgift: Deltagere fra Østdanmark: 400 kr.
Andre: 600 kr.

Introduktionskursus i onkologi for yngre læger

SKA har igennem det sidste års tid løbende arrangeret introduktionskurser for unge læger, der starter på de onkologiske afdelinger i Herlev, Hillerød, Rigshospitalet, Roskilde og Bornholm. Programmet er bredt sammensat og omfatter en oversigt over den kliniske onkologi i regionen samt en introduktion til strålebehandling og medicinsk kræftbehandling. Desuden præsenteres kursisterne for 'case stories', der fokuserer på såvel akutte medicinske/onkologiske tilstande som den understøttende behandling og palliation. Sidst, men ikke mindst, præsenteres kursisterne for en introduktion til 'den svære samtale' med kræftpatienten og dennes pårørende.

Kursusleder: Professor, dr.med. Heine Høi Hansen
Tid og sted: 19. januar 2008
Admiral Hotel, København
Kursusafgift: 300 kr.

SKA sekretærkursus: "Kræftsygdom og -behandling" - Modul II

Kurset henvender sig til sekretærer ansat på onkologiske afdelinger og er en fortsættelse af modul I.

Da kurset traditionelt har stor søgning, anbefaler vi interesserede at sende registrering til SKAs sekretariat snarest muligt.

Kursusleder: Sekretær June Thygesen
Tid og sted: 5. februar 2009
Hotel Kong Arthur, Nørresøgade 11, Kbh. K
Kursusafgift: Deltagere fra østdanmark: 400 kr.
Andre: 600 kr.

SKA's kursusprogram - forår 2009

Ph.D. præsentationer – igangværende projekter

Dette er det 2. af to projektmøder, som SKA arrangerer i samarbejde med forsknings-udvalgene på onkologisk afdeling, Rigshospitalet og Herlev Hospital. På møderne præsenteres udvalgte ph.d. projekter, der efterfølgende diskuteres.

Møderne henvender sig til Ph.D.studerende, vejledere og andre læger ansat på østdanske onkologiske afdelinger.

Kursusleder: Professor, dr.med. Heine Høi Hansen
overlæge, dr.med. Dorthe Nielsen
overlæge, dr.med. Lena Specht
Tid og sted: Onsdag den 18. marts 2009, kl. 15.30-19.00
Hotel Admiral, København
Kursusafgift: 300 kr. inkl. middag (100 kr. uden middag)

Sorg og livsmod

Et kursus om sjælelige strabadser hos kræftpatienter og deres pårørende.

Kurset henvender sig primært til læger og sygeplejersker fra onkologiske afdelinger i direkte kontakt med kræftpatienter og deres pårørende.

Formålet med kurset er at give deltagerne viden om sorg hos efterlevende, om depression og eksistentiel lidelse hos kræftpatienter, og om livsmodets og håbets betydning for et liv med kræft.

Dag 1 underviser to internationalt anerkendte forskere i sorg, Margart Stroebe og Henk Schut, begge professorer i psykologi ved Utrecht Universitet, Holland. Stroebe og Schut har lanceret en teori, ifølge hvilken den sørgende skiftevis "arbejder med" og "holder fri fra" de mange følelsesmæssige, praktiske, sociale, kropslige, åndelige og kognitive vanskeligheder, der føler med at være pårørende til en kræftpatient. Dagen afsluttes med en perspektivering til danske forhold.

Dag 2 indeholder tværfaglige oplæg fra sygeplejerske, psykolog og præst, der vil tale om depression hos kræftpatienter, lidelse og mestring, livsmod og håb.

Emnerne er tunge, men handler til gengæld om det, der i høj grad optager de patienter, vi møder. Der vil være tid og plads til at diskutere alle emner i relation til egen arbejdssituation

Første undervisningsdag vil blive afholdt på engelsk.

Kursusleder: Psykolog Bo Snedker Boman og
sygeplejerske Hanne Skovfoged
Tid og sted: 16-17. april 2009
Admiral Hotel, København
Kursusafgift: Fastsættes senere, men afhænger af om du skal overnatte eller ej.

SKA's kursusprogram - forår 2009

Introduktionskursus i onkologi for yngre læger

SKA har igennem det sidste års tid løbende arrangeret introduktionskurser for unge læger, der starter på de onkologiske afdelinger i Herlev, Hillerød, Rigshospitalet, Roskilde og Bornholm. Programmet er bredt sammensat og omfatter en oversigt over den kliniske onkologi i regionen samt en introduktion til strålebehandling og medicinsk kræftbehandling. Desuden præsenteres kursisterne for 'case stories', der fokuserer på såvel akutte medicinske/onkologiske tilstande som den understøttende behandling og palliation. Sidst, men ikke mindst, præsenteres kursisterne for en introduktion til 'den svære samtale' med kræftpatienten og dennes pårørende.

Kursusleder: Professor, dr. med. Heine Høi Hansen
Tid og sted: 21. april 2009
Admiral Hotel, København
Kursusafgift: 300 kr.

SKA Kursus: Supportive Care – Modul I + II

Som noget helt nyt arrangerer SKA et 5 dages kursus i Supportive Care – understøttende behandling.

Den hastige udvikling inden for kræftbehandlingen og den dertil nødvendige understøttende behandling har de senere år udfordret det sundhedsfaglige personale på landets onkologiske afdelinger. Det er kursets formål at give deltagerne en evidensbaseret og opdateret indsigt i de vigtigste emner inden for den moderne kræftbehandlings behov for understøttende behandling. Fokus vil ligge på behandlingsrelaterede bivirkninger, samt psykosociale og rehabiliteringsmæssige forhold.

Kurset vil være delt i 2 moduler med ca. 6 ugers mellemrum. Formen vil være en blanding af katedralundervisning, gruppearbejde, sygehistorier og dialog samt kommunikationstræning.

Kurset henvender sig primært til yngre læger og sygeplejersker ansat på onkologiske afdelinger. For at få det fulde udbytte af kurset bør deltagerne som minimum have mere end seks måneders erfaring inden for det onkologiske speciale.

Kursusleder: Overlæge Svend Ottesen, Roskilde og
Hanne Skovfoged, sygeplejerske, SKA
Tid og Sted: Modul 1: 27-28. april 2009
Modul 2: 8-10. juni 2009
Hotel Kong Arthur, København
Kursusafgift: Fastsættes senere

SKA's kursusprogram - forår 2009

Praktisk onkologi for ansatte i medicinalindustrien

SKA arrangerer atter et 4-dages kursus i basal og praktisk onkologi for ansatte i medicinalindustrien.

Formålet med kurset er at give kursisterne en basisviden om karakteristiske forhold ved kræftsygdomme samt at tilbyde kursisterne et indblik i den praktiske kliniske onkologiske hverdag.

Kurset er delt op i teoridage og i klinikdage. Teorien foregår på Symbion Science Park, København, hvor underviserne vil gennemgå kræftsygdommens biologi, epidemiologi og patologi samt den medicinske og strålebehandlingsstrategi. Ydermere vil teoridagene bestå af en gennemgang af sygdomslære med fokus på 4-5 sygdomsgrupper og behandlingsmuligheder. Dag 4 indeholder desuden orientering om kliniske forsøg, etiske dilemmaer og klinisk forskning i praksis.

Klinikdagene foregår på de onkologiske afdelinger i Herlev, Hillerød, Roskilde og på Rigshospitalet. Hver kursist får en halv dag på et af centrenes onkologiske afdelinger, evt. med besøg i stråleafsnittet, og en halv dag på en onkologisk afd. i Roskilde eller Hillerød.

Kurset henvender sig til de ansatte i medicinalindustrien, der beskæftiger sig med onkologi.

Kursusleder: Overlæge, dr.med. Dorthe Nielsen, Herlev,
Sygeplejerske Hanne Skovfoged
Tid og sted: 11-14. maj, 2009
Symbion Science Park, Fruebjergvej 3,
2100 København Ø
Kursusafgift: 14.000 kr.

Sygeplejetemadag - *under udarbejdelse*

Kursusledere: Sygeplejerske Hanne Skovfoged
sygeplejerske Jane Elze Sannung
Tid og sted: 28. maj 2009 kl. 14.30-18.30
Lille Auditorium, Herlev Hospital
Kursusafgift: Deltagelse er gratis

Post ASCO Symposium

SKA arrangerer for 6. gang Post ASCO Symposium, der er den nationale opfølgning på ASCO's årsmøde.

På symposiet præsenteres højdepunkterne fra ASCO mødet inden for de store cancer sygdomme af en yngre dansk læge, suppleret af en senior læge, der som ekspert i den pågældende sygdom perspektiverer emnet.

Programmet omfatter øvre og nedre gastrointestinale tumorer, urologiske kræftsygdomme, gynækologiske tumorer, lungecancer, brystkræft samt hovedhals kræft og kræft i centralnervesystemet.

Det detaljerede program offentliggøres ultimo januar på SKAs hjemmeside, *www.skaccd.org*.

Kursusleder: Professor, dr.med. Heine Høi Hansen
Tid og sted: 19. juni 2009
Hotel Hilton / Københavns Lufthavn
Der er direkte adgang til hotellet fra terminal 3, hvortil toget kører. Bus 2A og 5A kører fra Rådhuspladsen til hotellet.
Parkering er mulig i lufthavnen mod betaling.
Kursusafgift: 400 kr for deltagere fra Østdanmark
500 kr. for øvrige Danmark
Andre deltagere bedes kontakte SKA sekretariatet ang. kursusafgift.

Internationale møder

2009

11-13. marts
Fourth International Conference on Translational Research and Pre-Clinical Strategies in Radiation Oncology
Geneva, Switzerland
www.iosi.ch/ictr2009.html

11-15. marts
NCCN 14th Annual Conference: Clinical Practice Guidelines & Quality Cancer Care
Hollywood, Florida
www.nccn.org

23-25. marts
7th International Symposium on Targeted Anticancer Therapies
Amsterdam, Netherlands
www.nddo.org (TAT 2009)

2-4. april
5th ISC International Conference on Cancer Therapeutics. Molecular Targets & Clinical Applications.
Barcelona, Spain
www.imedex.com

1-3. maj
European Multidisciplinary Conference in Thoracic Oncology (EMCTO)
Lugano, Switzerland
www.esmo.org

7-9. maj
1st IMPAKT Breast Cancer Conference: Improving Care and Knowledge in Translational Research
Brussels, Belgium
www.impakt.org

9-12. juni
Clinical Trial Statistics for Non Statisticians
Brussels, Belgium
www.eortc.be/seminar/educationpgm/stats2009/default.htm

20-26. juni
ECCO-AACR-ASCO Workshop: Methods in Clinical Cancer Research
Flims, Switzerland
http://www.ecco-org.eu/Education/Flims/FLIMS-10/page.aspx/414

24-27. juni
ESMO Conference: 11th World Congress on Gastrointestinal Cancer
Barcelona, Spain
www.worldgicancer.com

31. juli - 4. aug.
13th IASLC World Conference on Lung Cancer
San Francisco, CA
www.2009worldlungcancer.org

20-24. sept.
ECCO 15-34th ESMO Multidisciplinary Congress
Berlin, Germany
www.ecco-org.eu

27-29. nov.
Methodology of Clinical Trials in Oncology – 11th Central European Course
Vienna, Austria
www.esmo.org

2010

8-12. Oktober
35th ESMO Congress
Milan, Italy
www.esmo.org

SKA Uddannelsesaktiviteter forår 2009

Aktivitet	DATO September	Sted
	Januar	
Sekretærkursus nr. 4 – Modul I	14	Hotel Kong Arthur, København
Introduktionskursus for yngre læger i klinisk onk. i østdk.	19	Admiral Hotel, København
	Februar	
Sekretærkursus – Modul II	5	Hotel Kong Arthur, København
	Marts	
Ph.D. møde - igangværende projekter	18	Admiral Hotel, København
	April	
Sorg og livsmod	16-17	Admiral Hotel, København
Introduktionskursus for yngre læger i klinisk onk. i Østdk.	21	Admiral Hotel, København
Supportive Care - Modul I	27-28	Hotel Kong Arthur, København
	Maj	
Kursus i klinisk onkologi for medicinalindustrien	11-14	
Sygeplejetemadag	28	Herlev
	Juni	
Supportive Care - Modul II	8-10	Hotel kong Arthur, København
6. Post ASCO Symposium	19	Hilton

Læs mere på SKA's hjemmeside: *www.skaccd.org*

SKA ønsker alle en rigtig glædelig jul og et godt nytår.

Vi ses på et af SKA's kurser i 2009!