Wetenschappelijke vergadering NVNG: Theranostics in de lift

10 juni 2022

Ochtendprogramma

De wetenschappelijke voorjaarsbijeenkomst van de NVNG werd op 10 juni 2022 in Gelre Ziekenhuizen te Apeldoorn gehouden met als thema "Theranostics in de lift". Het was de eerste fysieke ontmoeting sinds het begin van de Covid-19 crisis in maart 2020. Na de welkomstwoorden van de voorzitter van de Commissie Wetenschappelijke Ontmoetingen (CWO) drs. Emilia Owers startte de eerste ochtendsessie van het door de CWO samengestelde programma onder voorzitterschap van dr. Marcel Janssen met een presentatie van nucleair geneeskundige prof. dr. Marnix Lam (UMC Utrecht) over "FAPI theranostics". Vervolgens behandelde nucleair geneeskundige drs. Dirk Wyndaele (Catharina Ziekenhuis Eindhoven) het onderwerp "Theranostics non-PSMA, non-dotatate…reflected". De laatste spreker van de eerste ochtendsessie was nucleair geneeskundige dr. Marcel Stokkel (NKI Antoni van Leeuwenhoek) met als presentatie "PRRT- from bench to practice and lesson for the future".

De tweede ochtendsessie, met dr. Hendrikus Boersma als voorzitter, startte met de presentatie "Development of ^{225}Ac-PSMA to support a phase 1 clinical trial" van ziekenhuisapotheker dr. Stijn Koolen (Erasmus MC). Vervolgens werd het onderwerp "Development of new production routes for existing and new isotopes" behandeld door dr. Karlijn Codee-van der Schilden (R&D Manager Medical Isotopes, NRG).

Sprekers van de eerste ochtendsessie: Marcel Stokkel, Marnix Lam en Dirk Wyndaele

Sprekers van de tweede ochtendsessie: Stijn Koolen, Karlijn Codee-van der Schilden en Robin Schellevis

De sessie werd afgesloten door dhr. Robin Schellevis (Licensing Manager SHINE) met de presentatie "Linear accelerator isotope production Groningen - radionuclide production". In de middag werden twee sessies gehouden met de presentatie van een vijftal vrije inzendingen zoals hieronder samengevat. Vóór het begin van het middagsprogramma werd een algemene ledenvergadering van de NVNG gehouden (zie bericht in aparte kader).

Samenvattingen vrije inzendingen middagprogramma

[18F]FDG-PET/CT in indeterminate thyroid nodules: health-related quality of life and cost-utility analysis

E.J. de Koster[1], O. Husson[3,4,5], M.O. van Aken[7], E.W.C.M. van Dam[7], L.T. Dijkhorst-Oei[8], L.F. de Geus-Oei[1,9,13], G.S. Mijnhout[14], R.T. Netea-Maier[2], W.J.G. Oyen[1,15,16], R.P. Peeters[17], A. Schepers[10], M. Snel[11], W.B. van den Hout[12], D. Vriens[9], for the EfFECTS trial study group

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Purpose

To evaluate health-related quality of life (HRQoL) and cost-effectiveness of an [18F]FDG-PET/CT-driven diagnostic workup as compared to diagnostic surgery, for thyroid nodules with Bethesda III/IV cytology. [18F]FDG-PET/CT accurately rules out malignancy and avoids 40% of futile diagnostic surgeries for benign Bethesda III/IV nodules.

Methods

Lifelong societal costs and HRQoL were assessed for 132 patients participating in the randomised controlled multicentre *EfFECTS* trial (NCT02208544) comparing [18F]FDG-PET/CT to diagnostic surgery. Longitudinal HRQoL assessment was performed using the EuroQol 5-dimension 5-level (EQ-5D-5L), the RAND 36-item Health Survey v2.0 (RAND-36), and the Thyroid Patient-Reported Outcome (ThyPRO) questionnaire on baseline, 3, 6, and 12 months, relative to the date of the [18F]FDG-PET/CT scan. The observed 1-year trial data regarding actual costs and quality-adjusted life years (QALYs) were extrapolated using a Markov model. The probability of cost-effectiveness was estimated using cost-effectiveness acceptability curves, taking uncertainty about sampling, imputation, and parameters into account.

Results

Patients randomised to active surveillance for an [18F]FDG-negative nodule instead of diagnostic surgery, reported stable HRQoL throughout the year. Univariate analysis indicated better HRQoL for patients undergoing surveillance than surgical patients with benign histopathology on multiple physical and psychosocial domains. Univariate within-group analysis suggested both temporary and continued HRQoL deteriorations in patients with benign histopathology over time. Multivariate within-group analysis demonstrated worsened HRQoL in patients with benign histopathology with regard to EQ-5D-5L utilities (p=0.001), RAND-36 physical functioning (p=0.04 and p=0.02), and ThyPRO cognitive impairment (p=0.01) and cosmetic complaints (p=0.02), whereas goitre symptoms (p<0.001) and anxiety (p=0.04) improved over time.

The observed 1-year cost difference of [18F]FDG-PET/CT as compared to diagnostic surgery was -€1,000 (95% CI: -€2,100 to €0) for thyroid nodule-related care (p=0.06). From the broader societal perspective, the 1-year difference in total societal costs was -€4,500 (-€9,200 to €150) (p=0.06). Over the modelled lifelong period, the cost difference was -€9,900 (-€23,100 to €3,200) (p=0.14). The difference in QALYs was 0.019 (-0.045 to 0.083) at one year (p=0.57) and 0.402 (-0.581 to 1.385) over the lifelong period (p=0.42). For a willingness to pay of €50,000 per QALY, an [18F]FDG-PET/CT-driven work-up was the cost-effective strategy with 84% certainty.

Conclusion

The reassurance of a negative [18F]FDG-PET/CT, indicating a benign

nodule, resulted in sustained HRQoL throughout the first year of active surveillance. Following the observed reduction in diagnostic surgery, an [^{18}F]FDG-PET/CT-driven diagnostic workup reduced the 1-year thyroid nodule-related and societal costs. It is very likely cost-effective as compared to diagnostic surgery for Bethesda III/IV nodules.

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[^{177}Lu]Lu-PSMA-I&T for treatment of metastatic castration resistant prostate cancer in routine clinical care

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Aim

[^{177}Lu]Lu-PSMA has been used for treatment of metastatic castration resistant prostate cancer (mCRPC). Clinical studies demonstrate safety and impressive efficacy of ^{177}Lu bound to PSMA-617. However, little data are available on the routine use of [^{177}Lu]Lu-PSMA-I&T. Our medical centre was one of the first in the Netherlands to start [^{177}Lu]Lu-PSMA-I&T therapy for routine clinical care, at the end of 2021. Treatment is given in 4 dosages of 7400 MBq with a 6 week interval. Aim of this study is to evaluate therapeutic efficacy of [^{177}Lu]Lu-PSMA-I&T in routine clinical care in mCRPC patients.

Patients and Methods

All patients were diagnosed with mCRPC and previously treated with androgen receptor-directed therapy (ARDT) and chemotherapy. Before treatment, patients underwent a [^{68}Ga]Ga-PSMA-11 and [^{18}F]FDG-PET/CT scan to determine eligibility for treatment with [^{177}Lu]Lu-PSMA-I&T. A follow-up [^{68}Ga]Ga-PSMA-11 scan was performed after 2 treatment cycles. [^{177}Lu]Lu-PSMA-I&T was prepared at our GMP certified radionuclide laboratory. Patients received questionnaires about quality of life (EORTC QLQ-C30 v3.0) and a form to evaluate pain (Visual Analog Scale, VAS), before every treatment and 4 weeks after their last treatment. Three questions regarding pain (range 0 - 10), health, and quality of life (range 1 - 7) were analyzed.

Results

Thus far, data of 9 patients, in total 18 dosages, have been used to assess effectiveness of this treatment. First dosage (n=9), second dosage (n=5), third dosage (n=3) and fourth dosage (n=1). Median pain score before treatment with [^{177}Lu]Lu-PSMA-I&T was 7 (range 1.5 - 8.5), (n=5). After 1 dosage of [^{177}Lu]Lu-PSMA-I&T, median pain score was 2, (n=5). After 2 dosages median pain score was 1 (range 0 - 2) (n=3). Overall pain response rate after the first dosage was 60 %. Improvement of quality of life was observed in 3 out of 5 patients. [^{68}Ga]Ga-PSMA-11 scan after 2 dosages showed improvement in 67% of the patients. PSA levels declined significantly (>50%) in 60% of patients as did the alkaline phosphatase levels. There was no dose limiting toxicity.

Conclusion

These preliminary results show that [^{177}Lu]Lu-PSMA-I&T is an effective and safe therapy for patients with mCRPC in routine clinical care. Both pain and quality of life are positively influenced and PSA levels show a significant decline. More extensive and updated results will be presented of this ongoing study.

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Sentinel Lymph Node Mapping in Breast Cancer Patients through Fluorescent Imaging using Indocyanine Green – the INFLUENCE trial

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Objective

To compare the (sentinel) lymph node detection rate of ICG-fluorescent imaging versus standard-of-care [^{99m}Tc]Tc-nanocolloid for sentinel lymph node (SLN)-mapping.

Summary Background Data

The current gold-standard for axillary staging in patients with breast cancer is sentinel lymph node biopsy (SLNB) using radio-guided surgery with a radioisotope of technetium, [^{99}mTc], sometimes combined with blue dye. A promising alternative is fluorescent imaging with the use of indocyanine green (ICG).

Methods

In this non-inferiority trial, we enrolled 102 consecutive patients with invasive early-stage, clinically node-negative breast cancer. Patients were planned for breast conserving surgery and SLNB between August 2020 and June 2021. The day or morning before

surgery, patients were injected with [^{99m}Tc]Tc-nanocolloid. In each patient, SLNB was first performed using ICG-fluorescent imaging, after which excised lymph nodes were tested with the gamma-probe for ^{99m}Tc-uptake ex-vivo, and the axilla was checked for residual ^{99m}Tc-activity. Detection rate was defined as the proportion of patients in whom at least one (S)LN was detected with either tracer.

Results

In total, 103 SLNBs were analysed. The detection rate of ICG-fluorescence was 96.1% (95%CI=90.4-98.9%) versus 86.4% (95%CI=78.3-92.4%) for [^{99m}Tc]Tc-nanocolloid. The detection rate for pathological lymph nodes was 86.7% (95%CI=59.5-98.3%) for both ICG and [^{99m}Tc]Tc-nanocoilloid. A median of 2 lymph nodes were removed. ICG-fluorescent imaging did not increase detection time. No adverse events were observed.

Conclusion

ICG-fluorescence showed a higher (S)LN detection rate than [^{99m}Tc]Tc-nanocoilloid, and equal detection rate for pathological (S)LNs. ICG-fluorescence may be used as a safe and effective alternative to [^{99m}Tc]Tc-nanocoilloid for SLNB in patients with early-stage breast cancer.

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(gepresenteerd door Peter Kaldeway)

Altered biodistribution of [^{68}Ga]Ga-DOTATOC during somatostatin analogue treatment

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Introduction

Staging and follow-up of low grade neuroendocrine tumours (NET) is preferably done with somatostatin receptor imaging with PET. However, therapy and imaging with somatostatin analogues utilize the same receptor. Although, the current guidelines recommend withdrawal of somatostatin analogues for 3-4 weeks prior to PET imaging, previous studies have shown a persistent decreased visceral uptake of DOTATATE after treatment (Gålne, A, J Nucl Med. 2019). For DOTATOC this has not been studied before. As DOTATATE and DOTATOC are comparable analogues, similar effects may be expected. The aim of this study was to assess the effect of clinical somatostatin analogue use on the biodistribution of ^{68}Ga-DOTATOC intra-individually.

Methods

The study retrospectively assessed 35 patients with metastatic gastroenteropancreatic-NET, who were treated with Lanreotide (a somatostatin analogue). All patients received a [^{68}Ga]Ga-DOTATOC PET/CT scan before and during treatment (FUP1). Some patients received an additional [^{68}Ga]Ga-DOTATOC PET/CT during Lanreotide treatment (n=19, FUP2). All scans were performed with a standardized protocol, administrating 2 MBq/kg of [^{68}Ga]Ga-DOTATOC 40 minutes prior to the scan. For each patient [^{68}Ga]Ga-DOTATOC uptake (SUVmax, mean) was assessed in both tumour lesions and normal tissue. Paired T-tests were performed to determine the differences between baseline and FUP scans. Results are presented as average ± standard deviation. Average follow-up interval between baseline and FUP1 was 15.9±18.4 months and between FUP1 and FUP2 was 10.4±5.5 months.

Results

Upon treatment the tracer availability in the bloodpool went up significantly (SUVmax baseline 0.99±0.44, FUP1 1.57±0.62 ,FUP2 1.51±0.56, $p<0.05$). This was accompanied by a lowered tracer accumulation in the liver (SUVmax baseline 5.97±1.59, FUP1 4.58±1.66, FUP2 4.95±1.55, $p<0.05$) and spleen (SUVmax baseline 21.17±7.11, FUP1 14.18±5.46, FUP2 18.85±5.68, $p<0.05$). There was a tendency towards an increase in tracer accumulation in spleen and liver between FUP1 and FUP2, though this was not significant. The accumulation in the uncinate process of the pancreas was variable, and not significantly different between baseline and follow-up scans. Interestingly the pancreas corpus and tail showed an increase in tracer accumulation during treatment and this effect was maintained in the second follow-up period (baseline 3.50±1.40, FUP1 4.38±2.48 and FUP2 4.70±1.65, $p<0.05$).
The tumor lesions did not show significant difference in tracer uptake, when compared to baseline.

Conclusion

Similar to previous findings with [^{68}Ga]Ga -DOTATATE, also with [^{68}Ga]Ga-DOTATOC the visceral binding (excluding parts of the pancreas) is significantly reduced after Lanreotide treatment, thereby increasing tracer availability in the bloodpool. There seems to be a small increase after second follow-up possibly indicating tissue somatostatin receptor upregulation after treatment, however this was not significant. Therefore, absolute comparison in lesions using the SUV on [^{68}Ga]Ga-DOTATOC-PET should be done with caution as the bio-distribution of the tracer after initiation of somatostatin analogue treatment is altered.

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(gepresenteerd door Femke Bemer)

PET-imaging and protein expression of the prostate specific membrane antigen in high grade glioma: a multi-center comparison study

Ilanah Pruis[1] and Sanne van Lith[2], Nelleke Tolboom[3], Tom Snijders[4], Dylan Henssen[2], Mark ter Laan[5], Maarten te Dorsthorst[5], Sandra Bossmann[5], Fleur Brienen[5], Pierre Robe[5], Philip de Witt-Hamer[6], Harry Hendrikse[6], Daniela Oprea[7], Maqsood Yaqub[7], Pieter Wesseling[8,9], Rutger Balvers[10], Clemens Dirven[10], Marion Smits[1], Martin van den Bent[11], Elsmarieke van de Giessen[11] and Sophie Veldhuijzen van Zanten[1]

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Introduction

Upregulation of prostate specific membrane antigen (PSMA) on neovasculature has been described in high-grade brain tumours, including glioblastoma (GBM), while vasculature in healthy brain shows hardly any expression of PSMA. This observation opened avenues for the application of radiolabeled PSMA-targeting molecules for positron emission tomography (PET) imaging. In the first clinical studies on the use of PSMA PET in glioma, moderate to high tumour-uptake was found. However, it is yet unclear whether this uptake is based on PSMA-specific binding to tumour-associated (endothelial) cells, or whether it represents aspecific accumulation/retention. In this multicenter PET study, we quantified dynamic uptake of various PSMA-tracers over time, in a series of de novo and recurrent high grade brain tumours, and correlated this to PSMA expression in tumor tissue obtained from subsequent biopsies.

Materials and methods

Fifteen patients, diagnosed with de novo (n=9) or recurrent (n=6) GBM underwent a PET scan upon injection of either 1.5 MBq/kg [^{68}Ga]Ga-PSMA-11 (n=7), 200 MBq [^{18}F]-DCFpyl (n=3) or 200 MBq [^{18}F]F-PSMA-1007 (n=5). Volumes of interest (VOIs) were drawn around the tumor using a 10-25% cut-off from maximal uptake, and a similar-sized VOI was drawn in the contralateral hemisphere (healthy brain, i.e., background). Tumour uptake and tumour-to-background ratios (TBR) were calculated. In 13 patients, tissue biopsies (n=40) were collected. PSMA RNA (n=5) or protein (n=11) expression, determined by sequencing or immunohistochemistry (DAKO, m3620, scoring 0-4), was correlated to tracer uptake on PET using Pearson or Spearman Rho analyses, respectively.

Results

In all patients, heterogenous moderate to high (SUVmax: 1.3-20.0) uptake was found, lasting up to several hours post-injection, irrespective of the used tracer. Uptake in contralateral healthy brain was low, with resulting high TB-ratios of 6.07-359. PSMA immunohistochemistry showed strong staining of tumour-associated endothelial cells, individual cells of unknown origin and neutrophils. No correlation was found, however, between PET uptake and IHC scores of either of these components (r = -0.1642, p = 0.3179), nor for PSMA RNA expression (r = -0.2830; p = 0.2710), while IHC scores and RNA expression did show strong correlation (r = 0.8228, p = 0.0016).

Conclusion

Our results indicate that PSMA tracer uptake in high-grade glioma on PET is at least partly aspecific, as no correlation with PSMA expression was found. The high TBRs for all PET lesions are, however, advantageous for imaging and promising for future PSMA-targeted radionuclide therapy in patients with high-grade glioma.

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(gepresenteerd door Ilanah Pruis)

Het CWO-najaarssymposium van de NVNG zal plaatsvinden op 7 oktober 2022 met als thema Nuclear Medicine: From Bench to Bedside in het Meander Medisch Centrum in Amersfoort. De vergadering is vooralsnog fysiek. Verdere details volgen op de internetsites van de NVNG en TvNG.

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Algemene ledenvergadering van de NVNG: voorzittershamer eindelijk overhandigd

De fysiek gehouden wetenschappelijke voorjaarsbijenkomst in Apeldoorn vond samen met een algemene ledenvergadering van de NVNG plaats. Een unieke kans om de hamer van het voorzitterschap te overhandigen. De huidige voorzitter van de NVNG Andor Glaudemans ontving de hamer uit handen van Marcel Stokkel, de vorige voorzitter. De vergadering werd gehouden in aansluiting op de ochtendsessie van de wetenschappelijke bijeenkomst van de NVNG.

Tijdens de Algemene Ledenvergadering van 10 juni jl. is Erik de Blois benoemd tot bestuurslid en is Christian Guillaume herbenoemd voor een tweede termijn als penningmeester. Daniëlle Vugts is uit het bestuur getreden.
De samenstelling van het bestuur van de NVNG is als volgt:

Prof. dr. A.W.J.M. (Andor) Glaudemans, nucleair geneeskundige, voorzitter
Drs. D.N.J. (Dirk) Wyndaele, nucleair geneeskundige, vicevoorzitter/beroepsbelangen
Dr. R.G.M. (Ruth) Keijsers, nucleair geneeskundige, secretaris
Drs. C.P.F. (Christian) Guillaume, ziekenhuisapotheker, penningmeester
Prof. dr. A.A. (Adriaan) Lammertsma, klinisch fysicus, bestuurslid/wetenschap
Prof. dr. W.J.G. (Wim) Oyen, nucleair geneeskundige, bestuurslid/Europa
Dr. L.M. (Lenka) Pereira Arias-Bouda, nucleair geneeskundige, bestuurslid/opleiding
Dr. ir. B.J. (Bart) Vermolen, klinisch fysicus, bestuurslid
Dr. R.H. (Erik) de Blois, klinisch radiochemicus, bestuurslid

Een aantal NVNG-bestuursleden tijdens de fysieke ledenvergadering van 10 juni 2022. Van links naar rechts: Christian Guillaume, Ruth Keijsers, Lenka Pereira Arias-Bouda, Bart Vermolen, Adriaan Lammertsma, Erik de Blois en Dirk Wyndaele. Achter, Martine van Loon van het Bureau NVNG.