PINTAD

The Pharma Imaging Network for Therapeutics and Diagnostics

Meeting Minutes

Topic	**The FDA Approval of ^{68}GA-PSMA-11 PET: an academic collaborative journey**
Date	29 January 2021
Speaker(s)	Jeremie Calais MD

Presentation content (see Dr Calais' slides on www.pintad.net)

Question and Answer Session 29-Jan-2021	
Topic	**Discussion**
Any thoughts on beta vs alpha emitters for the radiotherapy side of the treatment?	Alpha much higher energy deposition and double strand DNA damage incidence. Much higher anti-tumor effect than lutetium. Severe xerostomia is the main side-effect due to high uptake in salivary glands. Some work has been done to mitigate the side effects to an acceptable level. Under 100MBq/kg it seems to be manageable. The main limitation is the limited supply chain, especially for a high incidence cancer such as prostate cancer. Some people/companies are working on establishing a high capacity production of actinium.
From your experience at what PSA value would you recommend a patient have a PSMA PET in biochemical recurrence?	Clearly the PSA level is correlated to the positivity rate (see slide #042) For early biochemical recurrence after surgery, I would say that the chance to see something at PSA 0.2 is around 25%. So if it is free, I would say go for it, nothing to lose. Now paying 3300 USD out-of-pocket is a different story. We get a higher chance to see something maybe a PSA of 0.3-0.4 would be better. On the other hand, It has been showed that a negative PSMA PET has a good prognostic value for SRT outcome. (https://pubmed.ncbi.nlm.nih.gov/31676727/) And the earlier you start SRT the better result you get.
Can you give a sense of the effort needed for an academic institution to get abbreviated NDA approval to use 68GA PSMA?	The work will focus mainly on the CMC section. The radiochemist/radiopharmacist/cyclotron team will have to establish a setup that can show the same final product 68Ga-PSMA-11 with the same manufacturing methods. Consulting companies can help to put together the submission package. Details here: https://doi.org/10.2967/jnumed.120.260455 https://doi.org/10.2967/jnumed.120.260455

PINTAD

The Pharma Imaging Network for Therapeutics and Diagnostics

Presentation content (see Dr Calais' slides on www.pintad.net)

Question and Answer Session 29-Jan-2021	
Topic	**Discussion**
How far are we from commercial solutions?	NDAs submitted by Progenics (18F-DCFPyL) and Telix (kit based method for 68Ga-PSMA-11). Possible in Q3/Q4 2021? https://telixpharma.com/news-media/telix-new-drug-application-for-prostate-cancer-imaging-product-accepted-by-us-fda/ https://investor.lantheus.com/news-releases/news-release-details/lantheus-holdings-submits-new-drug-application-us-fda-pyltm-18f
Were there any studies done when the primary tumor was positive and biopsied?	Not the data used for the NDA. A lot in pubmed ! Please specify your question(s).

Additional Post-Meeting Submitted Question and Answers	
Topic	**Discussion**
Could you please comment on FDA's viewpoint of incorporating PSMA-PET findings to modify risk stratification in clinical trial of therapeutic regimen?	I believe the FDA would be interested to have therapeutic clinical trials that integrate PSMA PET in the selection and/or stratification of patients. It will be easier to do when approved and easily available everywhere.
Is there any additive value of combined 68Ga-PSMA-11 PET and MRI for primary prostate cancer detection, local recurrence detection after focal therapy, extra-capsular spread-seminal vesicles invasion and localization compared with multiparametric MRI?	Yes. There is always a part of the tumor lesion that is missed by PSMA PET and a part that is missed by MRI (only 40-60% of overlap) PSMA PET may be more sensitive to detect additional foci, bilateral disease or T3 disease (always toward T-upstaging). But the spatial resolution is too low, and the intra-prostatic read is difficult and therefore reader-dependent. So, for local T-staging PSMA PET/MRI is the best when available. Otherwise, MRI is clearly more robust and reliable than PSMA PET/CT. PSMA PET/CT should be used when MRI and/or biopsy are inconclusive/negative. PSMA PET/CT is the best for N and M staging.
From FDG PET we know any SUV change is directly related to metabolism. How is a	Multiple parameters. PSMA density/quantity can be related mostly just to the quantity of the tumor cells (ex: after surgery, radiotherapy, chemotherapy) and

Additional Post-Meeting Submitted Question and Answers	
Topic	**Discussion**
change in SUV related to this surface/membrane PSMA ligand be seen? Does an SUV increase mean growth, worsening in that lesion, treatment failure? Is it comparable?	therefore represent a good surrogate marker of the quantity of tumor cells. BUT PSMA expression is in a complex relation with the up/down-regulation pathways of the Androgen Receptor. So any therapy that interacts with AR or PSMA will impact the PSMA expression and not linearly reflect the amount of cancer cells. 1. Initial staging, Treatment naïve disease, first line of ADT: decreasing uptake under ADT (response to ADT). So any In castrate sensitive setting, ADT will decrease the signal (and the size of the tumor lesions) significantly after a couple of weeks. So the sensitivity of the scan will be decreased significantly 2. Castrate Resistant disease under first line ADT: increasing uptake indicating resistance/recurrence 3. Castrate Resistant disease starting new AR-targeted therapy: short initial increase of PSMA expression (variable in time and intensity) followed by response and PSMA uptake decrease (long term) 4. Progression under new AR-targeted therapy: increasing uptake indicating resistance/recurrence