Response to LuPSMA Enquiry
ACPSEM Email Service

Dear Members,

I read in today's paper the good news of how a terminal ill prostate cancer patient had received a further extension in his life by a radiopharmaceutical substance (named LuPSMA). The treatment showed very encouraging results for this patient with widespread secondary prostate cancer. Please read:

https://www.smh.com.au/national/from-lucas-heights-to-petermac-new-prostate-therapy-is-a-game-changer-20180508-p4ze1f.html

From Lucas Heights to PeterMac, new prostate therapy is a game-changer

www.smh.com.au

Experimental treatment, ignored by big pharma companies, and being trialled at Melbourne's Peter MacCallum Cancer Centre has had some 'very exciting' results.

Congratulations to all involved in this work. It says Peter MacCallum Hospital and Lucas Heights are involved. Are some of our members involved?

If so, I would be interested in speaking with them. I would love to have a short article for our new Foundation Website (it's in the final stage of development).

There's been much talk by the profession wanting to raise its public profile.

The Foundation's website is where your professional profile can be effectively promoted widely. Articles by our members, geared to provide our particular aspects with up-to-date information for the public, patients, sponsors, Government administrations and even our members. The web will have articles, blogs and a place for patients to comment and ask questions.

It covers all aspects of physics, engineering, radiopharmacy or any other related science or biology applied to medicine. It will seek contributions and subscription from as wide an audience as possible. It will encourage participation of degree, technical and company personnel with the needs of our patients as being the focus.

The website gives a lengthy version of what the Foundation Board finally agreed as its vision, aims, etc.. The attached is a summarised version to assist me with the website development.

I have volunteered to get the Foundation Website up and going. But, once that's done, it will need support by your leaders in your various areas of the profession to generate the material and enthusiasm necessary to make it a viable enterprise. The Foundation Chairman, Dr Sean Geoghegan will make the formal approach to the College for this to begin.

Once the website is visible and underway, The Foundation is proceeding to the next challenge in raising solid financial support for initiatives. The website is the 'showpiece' to get external supporters.

So, if there are similar improvements in techniques or technology, then please keep in mind the new Foundation website as an excellent place to promote your valuable work. You can always contact me and discuss this further.

Yours sincerely,

Lyn Oliver AM PhD, 9 May 2018
drlynoliver@me.com

Barry Allen

Without being too negative, the facts are that this is a "me too" study of the type that Australian nuclear medicine and Ansto are famous for. LuPSMA was certainly effective and an advance on current therapies.
The German study alluded to in the article used this conjugate and also showed unequivocally that targeted alpha therapy with AC225 was markedly superior to targeted beta therapy with Lu177.
We published a review in a high-ranking journal this year that showed, in every preclinical and clinical case, that alpha therapy was superior to beta therapy (although its long been obvious that this is the case). As such, using beta radiation could be considered to disadvantage the patient and therefore be unethical.
Last year we proposed a phase 1 clinical trial of targeted alpha therapy for castrate resistant prostate cancer with our own targeting vector which was considered to be lethal by one reviewer, so we didn't get the NHMRC grant. (what's new?)
However, hopefully, there is a medphys at PMCI who played an important dosimetry role in this work.
Barry

Roger Price

Thanks for this useful exchange. I have spared the rest of ACPSEM my small contribution.

Lu-PSMA-617 is rapidly becoming one form of standard of care for castrate-resistant prostate cancer Rx, thanks in part to the TheraP study driven by Peter Mac (Hofman et al) and the ANZUP Cancer Trials Group – and to some extent to the private sector (eg; Theranostics). Australia is not a world leader in molecular radiotherapy (MRT, by which I mean targeted radiotherapies), despite available expertise and despite Barry and his colleagues' key contributions over the years – EBRT related studies have I guess been a priority of funding in the past – and Australian society in general is destructively risk-averse to innovation. We definitely need more of Barry's wisdom. It would be expected that some patients will soon emerge whose disease (following a short period of optimism) is resistant to Lu-177-PSMA ligand therapy, and targeted alpha Rx is the obvious next consideration. Ra-223 chloride won't do the entire trick because it attacks bony mets only – albeit pretty effectively. Here in SCGH (part of ANZUP collaboration via our NM Dept) our group is starting to scope this, expecting to expand our Lu-177 work, but hoping to stay ahead of the game – when the clinicians come knocking at our door.

ANSTO does have an important role in this, though the cost of their Lu-177 is a bit steep – comparatively. That said, they are funding isotope for the TheraP study – which is key contribution.

A segue note of appreciation for the ACPSEM. Without their 'debugged' TEAP training model (DIMP, ROMP) and their financial, political and other input in recent years, trainee radiopharmaceutical scientists (RPS) would have no (predominantly) federally funded certification pathway, backed by a learned society that actually cares. This new certification will radically transform the quality and national professional standing of this craft – and is already clearly doing so already in WA. More will be said about this at EPSM 2018.

Regards
Roger

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Lu-177 Rx for prostate cancer is indeed an excellent example of how both ‘big science (i.e.; OPAL), medical physicists and the new ACPSEM-midwifed category of radiopharmaceutical scientists are all putting their shoulders to the wheel, to translate and refine a genuinely new (to Australia) therapeutic modality.

That said, I think Barry has some right to be a bit cynical – he has been contributing in this general area for a long time, but has I suspect been a bit of a voice in the wilderness. He should take heart however that his voice may have more heft in the future, as mainstream thinking becomes more acclimatised to his topic. In fact, having written a chapter (yet to be published) on the physics of MRT a couple of years ago, I have noticed that only recently – and indeed driven to a fair degree by the Lu-177 prostate story – has MRT reached the front row of interest in some boutique cancer therapies. (A pet interest of mine is in hybrid MRT plus EBRT therapies [considered together via radiobiologically-informed common dose platforms such as BED], but the evidence that these will become widespread is yet to be assembled). Also, interesting though MRT is for disseminated disease, the number of patients it benefits in the total ‘cancer Rx space” is small compared with traditional treatment modalities – and may remain so. For example, MRT Rx for advanced castrate-resistant prostate cancer costs about $30k for isotope alone (5 consecutive treatments). Of course, if you are one of those lucky ones…!

However, there needs to be more discussion. I get a bit tired of advocacy for - say – Cu-67 as a basis for treatment. It has great qualities, but what is the use of therapy that can only ever treat a handful of cases because of scarcity of isotope? So, yes, a very interesting niche area – particularly since it has provided hope in cases where there are virtually no other options (for example also, metastatic neuroendocrine tumours, and of course forms of lymphoma etc) but it will not turn the world of oncology up-side down – unlike maybe the emerging (non-radioactive) T-cell checkpoint inhibitor therapies.

Lyn, if only we were 30 years younger (as noted earlier, I retire at the end of this year) – we would be hurling ourselves into all this stuff!

Cheers
Roger

Price Jackson

Hi Lyn,
There are certainly many people involved in this type of trial. It's really a credit to the hard work of the clinicians and radiopharmacists who have put together a practical, well-monitored protocol that may be adapted at other Australian Centres. As the SMH article alluded to, one of the great successes has been in ANSTO developing a local supply line for Lu-177 which should make it feasible to build a broader referral base for prostate cancer patients who may benefit from this type of targeted therapy in the future.

As a physicist, I've been involved in monitoring radiation dosimetry as part of the LuPSMA trial using post-treatment imaging. A unique aspect of radionuclide therapy in comparison to other systemic treatments is that we can produce, with a certain degree of precision, a map of the agent's likely effect based on an individual's biodistribution of the tracer. One of the secondary aims of the LuPSMA study is to test for radiation dose-response relationships which might provide a rationale to perform patient-specific activity prescription to better optimise treatment in the future. It's an exciting project that involves the development of new computational tools and we hope will have a tangible impact on patient management.

The trial has already garnered quite a lot of publicity so I'm hesitant to stoke the fires any more, but if you think something like that would be interesting to discuss I'm happy to contribute however might be helpful.

Price Jackson, PhD
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Hi Lyn,

Thanks for your interest in this. My department (Nuclear Medicine, Sir Charles Gairdner Hospital, Perth) will be involved in the nationwide 'TheraP' trial which includes a Lu-177 PSMA treatment arm (50%). As far as I know, the Dept of Nuclear Medicine at Fiona Stanley Hospital (Perth) is also participating. This trial is being driven by Peter Mac in Melbourne, where Price Jackson is the physicist to speak to (Price.Jackson@petermac.org). There are no full ACPSEM members here at SCGH (I'm only an associate member and we have one or two TEAP trainees) but at Fiona Stanley the medical physics contact is Jan Boucek (Jan.Boucek@health.wa.gov.au), who may be a full member.

It is worth noting that Lu-177 PSMA therapy is not yet TGA-approved and hence is only available through the Special Access Scheme. It is being provided privately across Australia (e.g. there is a WA-based company called Theranostics Australia doing it: http://theranostics.com.au/lutetium-psma-therapy/) and there is concern that patients not randomised to the LuPSMA therapeutic arm of the TheraP trial will simply drop out and seek LuPSMA private therapy, such is the demand, which will compromise the trial and hence slow the introduction of the therapy to the public system.

Medicine and politics...

Cheers,
Paul

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Lutetium PSMA Therapy, or Prostate-Specific Membrane Antigen Therapy, is a specific type of treatment used for people with advanced prostate cancer.