177Lu-PSMA-617 for metastatic prostate cancer in India

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177Lu-PSMA-617 in metastatic castrate resistant prostate cancer

Metastatic castrate resistant prostate cancer (mCRPC) has a 5-year survival rate of 35%.[1] Indian statistics are significantly worse than high income countries (HICs) with crude mortality at 4.5/100,000, projected to double by 2040.[2] Lutetium vipivotide tetraxetan (177Lu-PSMA-617) or Pluvicto by Novartis, in March 2022, became the first US FDA approved radioligand therapy (RLT) in mCRPC to treat disease progression on androgen receptor signaling inhibition (ARSi) and taxane-based chemotherapy. The recommended dose being 7·4 gigabecquerels (GBq; 200 mCi) intravenously every 6 weeks for up to six doses or until disease progression or unacceptable toxicity.[3] In an era of resource stratification and bridging disparities between HICs and low-middle-income countries (LMICs), the Pan-Asian version of the ESMO practice guidelines in July 2022 provided a 100% consensus of 177Lu-PSMA-617 administration based on the US FDA approval.[4] Following this was a strong recommendation from the Urological Society of India guidelines in October 2022.[5]

Radioligand therapy centres–practical challenges for India and LMICs

RLT Centres delivering 177Lu-PSMA-617 make a promising industry although cost-benefit analyses before integration into standard practice is imperative. Rising demand for production, adaptation of hospital infrastructure, associated costs of handling and disposal restrict it to private tertiary centres at exorbitant costs with scarce availability in public funded systems, including a select few in India.[6,7] For example, RLT centres must have isolation wards connected to large decay tanks for collecting radioactive toilet waste. Recently, the Atomic Energy Regulatory Board (AERB) has permitted to carry out radionuclide therapy in dedicated wards with attached toilets for patients such that plumbing lines from this toilet may be directly connected to the main sewerage with no need of decay tank. India has just over 90 isolation wards with around 200 hospital beds at present.[6,7]

In the US healthcare setting, treatment costs of 177Lu-PSMA-617 in mCRPC was double that of standard of care ($169,110 vs $85, 398). The incremental cost effectiveness ratio was > $200,000 per quality adjusted life years.[8] Having said that, the precise place for 177Lu-PSMA-617 in the mCRPC treatment landscape remains unclear. On one hand is the phase III VISION trial's relative lack of a control arm and the universal prior use of an ARPI (100%) and docetaxel (97.9%), which remain standard early therapies in mPC[9]; on the other is 177Lu-PSMA-617's comparison against cabazitaxel in phase II TheraP which showed no overall survival benefit but increased cost.[10] Not only being more costly than cabazitaxel, the maximum cost per cycle of 177Lu-PSMA-617 to remain cost-effective is $38,826 USD.[8] Currently, around 10,000 to 15,000 doses of 177Lu at 7.4GBq are administered annually and there is already a significant shortage. 177Lu production requires highly specialized high-flux neutron facilities.

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Current nuclear reactor facilities cannot be relied upon for uninterrupted supply while construction of new ones demands at least 10 years.[8]

India has a unique scenario of comparatively reduced cost of treatment due to indigenous production, unlike other LMICs. Although private medical insurance is gaining speed, out-of-pocket healthcare remains dominant. The exponential growth in its theranostics over the last decade was due to the availability of in-house radioisotopes and radiopharmaceuticals from the Bhabha Atomic Research Centre (BARC). This is India's only national public funded agency with Lu177 production facility.[11] Lutetium chloride (177LuCl3) is produced in BARC reactors which can be directly used for labelling PSMA or DOTATATE/Lutathera (for neuroendocrine tumours).[12] In a significant development, single vial freeze dried kits of these are available.[13] Presently, the Board of Radiation Isotope Technology (BRIT) is supplying both 177LuCl3 for labelling radioligands and using in hospital nuclear pharmacies as well as prelabelled Lu-177 PSMA.[12,13]

The cost of 100 mCi of labelled 177Lu-PSMA-617 is 80,000 INR which when superimposed onto investigation and admission costs, amounts to around 125,000 INR per cycle.[11] Whilst a published Indian health economics model does not exist, it must be reinstated that Mehrens et al.'s American experience is neither comparable nor applicable. The intent of use of the Indian product is different, i.e., without commercial angles. Although another source is imported 177Lu-PSMA-617 from Isotope Technologies Munich SE (ITM), Germany which is the world's largest Lu177 production facility, a higher cost (around 250,000 INR) is incurred, courtesy obvious commercial incentive.[11] This in context, no direct comparison on the cost-efficiency of the German imported vs Indian in-house products prevails, as we believe is not ethical due to the intent in their economics. However, the safety and efficacy of these have been established in existing literature published from India.

Future directives for LMICs

The increasing unmet demand coupled with challenges of finance and infrastructure are a pressing concern for use of 117Lu-PSMA-617 RLT on a larger scale. Sustainable goals should include–1) strategizing against financial and infrastructural constraints i.e., increasing indigenous production of radionuclides and kits; 2) assessing the safety profile of these therapeutic radionuclides in conjunction with nuclear regulatory boards to administer them on day-care basis at institutions lacking isolation wards. Given good acceptance of theranostics in India for neuroendocrine tumours with Lu177-DOTATATE, adding Lu177-PSMA in the same centre may alleviate logistic and financial toxicity, both on public and private ecosystems. Moreover, a significant expansion in the nuclear medicine battalion with frequent multidisciplinary meetings may increase awareness among clinicians about their safety and efficacy so that it can be considered in earlier stages of disease rather than advanced stages already heavily pretreated with prior lines alongside major financial drainage. Lastly, further studies on 177Lu-PSMA-617 with larger cohorts and longer follow up periods are necessary to convince policy makers to invest in dedicated RLT centres for the large daily operational expenditure and even larger capital. In essence, a low cost, high throughput solution for increasing affordability and accessibility and decreasing global health inequalities comprises the unmet need of the hour. This is also a call for resource stratification, implementation, and capacity building in low resource settings.

Contributors

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Declaration of interests

None declared.

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