A Pipeline Analysis of Immuno-Oncology Medicines - Pembrolizumab, Nivolumab, and Atezolizumab

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Background

Immuno-oncology, also known as cancer immunotherapy, is a form of cancer treatment that uses the body's own immune system to prevent, control, and eliminate cancer. Using the immune system has the greatest potential for the specific destruction of tumours with no toxicity to normal tissue and for long-term memory that can prevent cancer recurrence. As monotherapies or combinations, these approaches are having a substantial impact on the treatment of some patients with advanced, previously untreatable, malignancies- improving the prognosis for many patients.(1)

This horizon scan aimed to provide a comprehensive overview of future indications for the selected immuno-oncology pipeline products: pembrolizumab, nivolumab, and atezolizumab. The outputs from the scan will deliver the insight needed to support decisions about the reality and impact of adopting new immuno-oncology indications within the NHS and assist with investment decisions.

Methods

The NIHR Innovation Observatory (IO) undertakes routine horizon scanning as part of its core function, utilising a robust methodology to identify and track innovative health technologies. It maintains a comprehensive internally facing database – MInD ('Medicines Innovation Database') – of these innovative medicines, focusing on those with potential UK/EU license/launch within ~3-5 years. MInD contains individual 'Technology Records', defined as innovative medicine(s) + indication(s) that triangulates intelligence from 'hard' data sources such as clinical trials, 'soft' intel such as news/media, and 'pharma' intel such as press releases and direct engagement with companies.

This project initially included records from MInD containing pembrolizumab, nivolumab, or atezolizumab, and excluded those with non-oncology indications, phase I trials, and those with no plans to launch in the UK. A revised inclusion criteria then focused on phase III trials and excluded records where our target products were not considered the primary treatment. Data were extracted May 2022.

Results

Overview

- 43% of records were for pembrolizumab, 38% for nivolumab, and 19% for atezolizumab (figure 1)
- Combination therapies were more common (95%) than monotherapies (5%)
- 604 records were found to only have industry sponsors, with 102 being only investigator initiated, and 446 having a mixture of both sponsors
- Phase II trials were most common across each product investigated (47%), followed by phase III (21%) (figure 2)
- The initial inclusion criteria resulted in 1152 records being identified, this was further condensed to only include records in which phase III was the highest level of development and excluded records where pembrolizumab, nivolumab, and atezolizumab wasn't the primary treatment, resulting in 68 records clinicians deemed most significant to the pipeline in the coming years

Therapeutic Area

- Lung and respiratory cancers were the most investigated with 189 records, followed by multiple areas, and gastrointestinal cancers (figure 3)
- Some therapeutic areas such as head and neck cancers, haematological cancers, neurological cancers, and sarcomas had no records at phase III development (figure 4)

Stage of disease

- Metastatic / unresectable cancer was most commonly investigated

Place in treatment

- First line treatments were most prevalent across all records

Mutations/ subgroups

- The breast cancer therapeutic area had the most named mutations, with triple negative being most common

Discussion

- The initial inclusion criteria provided a broad horizon scan of the pipeline for the products pembrolizumab, nivolumab, and atezolizumab. Discussions with clinical experts on how the data could best be used resulted in the final inclusion criteria, in which the data would be more relevant to decision making for policy and funding in the immediate future.
- Examining the final included data set in more detail showed that therapeutic areas such as neurological cancers and sarcomas had no late-stage development, highlighting a gap in clinical development.
- Combination treatments are most widely studied which could reflect that these products have been licensed as both monotherapies and combinations for several years internationally.
- Challenges in the project included standardisation of the data fields for analysis, and collating the most relevant data fields that would be most useful for future decision making.
- Horizon scanning can lack weighting of evidence and may not give an exhaustive summary of current evidence due to the early stage in which the data is collected(2). The dataset provided an initial 'spine' of data to the NHS and accelerated access collaborative (AAC) – further stakeholder (clinical and commercial) and enrichment activities of the dataset are continuing to translate the data into actionable intelligence that will help contextualise the data into future clinical pathways.

Graphs

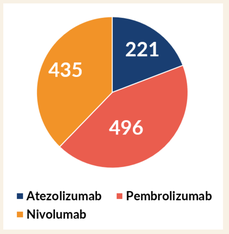

Figure 1- Number of records included for each immuno-oncology product

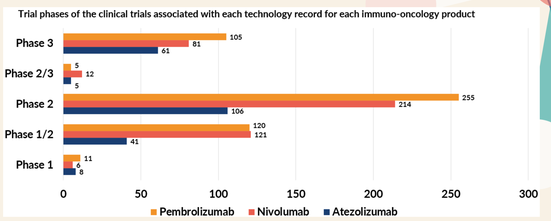

Figure 2– Number of records in each stage of clinical development for each immuno-oncology product

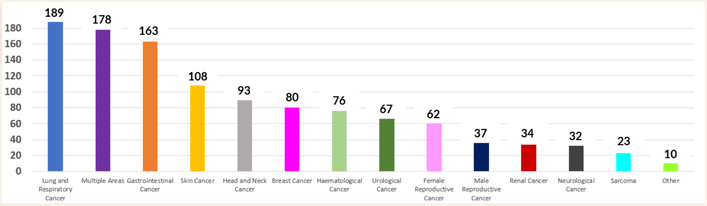

Figure 3- Number of records identified in each therapeutic area (initial inclusion criteria)

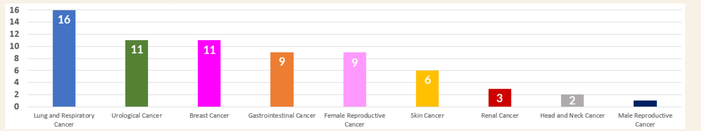

Figure 4- Number of records identified in each therapeutic area (final inclusion criteria)

Conclusion

The horizon scan identified areas of significant development activity for the immuno-oncology medicines which will help to influence preparation for future licensing reviews and policy decision making, improving the efficiency of the process, and potentially reducing time to market. The scan presents an initial dataset which requires further breakdown into different therapeutic areas to understand potential changes in future clinical pathways, and has helped to highlight gaps in research.

References

(1)Finn OJ. Immuno-oncology: understanding the function and dysfunction of the immune system in cancer. Ann Oncol. 2012;23 Suppl 8(Suppl 8):viii6-9. Available from: https://doi.org/10.1093/annonc/mds256.
(2)Malin Nuth W-S, Gloria T, Eli F. Barriers and facilitators to adopting horizon scanning to identify novel integrated care models: a qualitative interview study. BMJ Innovations. 2022;8(2):65. Available from: https://doi.org/10.1136/bmjinnov-2021-000804.

Disclaimers

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