THE HORIZON OF ONCOLOGY: ESTIMATING THE IMPACT OF NEW EU REGULATION ON HEALTH TECHNOLOGY ASSESSMENT FOR 2025-2028

HPR11

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Introduction

In January 2022, the new Regulation (EU) 2021/2282 on Health Technology Assessment (HTAR) was adopted by the European Commission with the aim to harmonize the quality of evidence generation among European countries, reduce duplication of efforts for HTA bodies and industry, and improve the rapid and widespread availability of medicinal products across Europe.[1]

As part of the HTAR, starting from 12th January 2025, all oncological New Therapeutic Entities (NTEs) and advanced therapy medicinal products (ATMPs) applying for Marketing Authorization (MA) will undergo the Joint Clinical Assessment (JCA). This will also apply to any requests for extension of indication of these NTEs.[2]

The JCA entails a mandatory scientific assessment of the relative clinical effectiveness and safety of a medicinal product compared to its competitors, based on a defined assessment scope relevant to all Member States.[2]

The introduction of the JCA establishes standards that may vary from national requirements, highlighting the need for a thorough comprehension of the new system to align EU and national evaluations, ensuring transferability of EU JCAs results to national processes.[3]

While national Authorities are preparing for a change in the ways of working for evidence assessment of these products, the purpose of this study was to estimate the number of NTEs that will undergo JCA procedures during the early stages of implementation of the new Regulation. This will include oncological and oncohematological NTEs that will submit a MA application between 2025 and 2028 and their extensions of indication.

Methods

In order to estimate the number of oncological and oncohematological NTEs that can be expected to submit a MA application between 2025 and 2028 and their extensions of indication, the analysis was conducted on all active clinical trials involving antineoplastic medicines.

Data were retrieved from the IQVIA Pipeline Link database, that collects pipeline projects for approximately 600 diseases across 75 countries, detailing features as disease, therapeutic class, and regulatory status.

Given the time lapse considered, only phase II and III clinical trials were selected, excluding phase I studies due to their prolonged timelines and lower success probabilities for drugs in early research stages.

In accordance with the HTAR[2], among all oncological and oncohematological medicines in phase II or III of clinical development, the analysis focused on medicines being studied for their first indication. This was initially done by excluding medicines already approved or being studied for supplementary indications, and biosimilars. For medicines involved in multiple clinical studies, the trial for the primary indication was identified, selecting the most advanced phase trial or the earliest started study.

Among these, the NTEs that could submit a MA application between 2025 and 2028 were identified, based on the median time from trial start date to EMA submission, derived from historical data from an IQVIA database on Italian negotiation dynamics.

Given the Likelihood of Approval (LoA) for oncological and oncohematological NTEs retrieved from literature[4], the number of NTEs that might undergo EMA evaluation directly from phase II or phase III studies was estimated. In particular, the likelihood of FDA approval[5] was used as a proxy. It was assumed that these rates would also be applicable to EMA approval, as EMA and FDA reportedly have a high concordance (up to 98%) in their marketing authorization decisions.[5]

Furthermore, the number of the NTEs currently in phase II trials that could advance to phase III and apply for a marketing authorization by 2028, were estimated considering the median duration of oncological phase II studies,[6] the Probability of Transition (PoT) in phase III retrieved from literature[4], and the time required for EMA submission.

Lastly, an estimate was made of how many of the selected NTEs might undergo the JCA process for subsequent indications by 2028. Considering all oncological and oncohematological molecules with a positive CHMP opinion for their first indication between 2015 and 2019, the number of their approved indications in a 4-years time horizon was retrieved. This historical trend was used to estimate the number of approval requests for new indication that might be submitted for the selected NTEs by 2028.

Results

As shown in *Figure 1*, the analysis of the IQVIA Pipeline Link database showed that 4,520 clinical studies were in progress at the time of data extraction, with oncological and oncohematological trials accounting for 45% (2,046) of these studies. Among them, 854 phase II and 434 phase III clinical studies were in progress.

Among all oncological and oncohematological medicines being studied, 639 NTEs under development for their first indication were identified, with about 20% involved in phase III and 80% involved in phase II clinical studies.

Elaborating on an IQVIA database on Italian negotiation dynamics, a median time from trial start date to EMA submission of 3.5 years was observed for both phase II and phase III studies, and oncological and oncohematological drugs. This led to the identification of 320 oncological NTEs in development that could undergo EMA evaluation between 2025 and 2028, including 261 for solid tumors and 59 for hematological cancers. Based on the likelihood of approval (LoA) for phase II oncological (6.3%) and oncohematological (13.1%) drugs, we estimated that 11 oncological and 6 oncohematological NTEs might undergo EMA evaluation directly from phase II studies by 2028, whereas 9 drugs could transit from phase II to phase III studies. Considering all drugs in phase III (those transiting from phase II and those already in phase III) and applying the LoA for phase III oncological (27.3%) and oncohematological (45.4%) drugs, it was estimated that 25 oncological and 7 oncohematological NTEs could potentially undergo EMA evaluation from a phase III study by 2028.

Overall, 49 new oncological entities are estimated to undergo JCA process between 2025 and 2028 (*Figure 2*).

Lastly, by applying the historical trend on the rate of new indications, it was estimated that 30 additional evaluation processes will be undertaken for extension of indication by 2028, with a total of 79 JCA processes to be carried out between 2025 and 2028 (*Figure 2*).

Figure 1. ***Number and characteristics of drugs in clinical development as of June 2024***

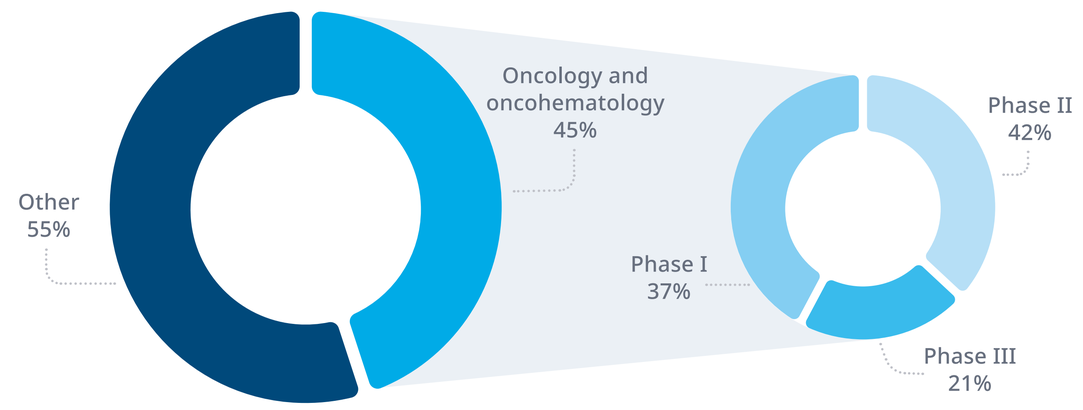
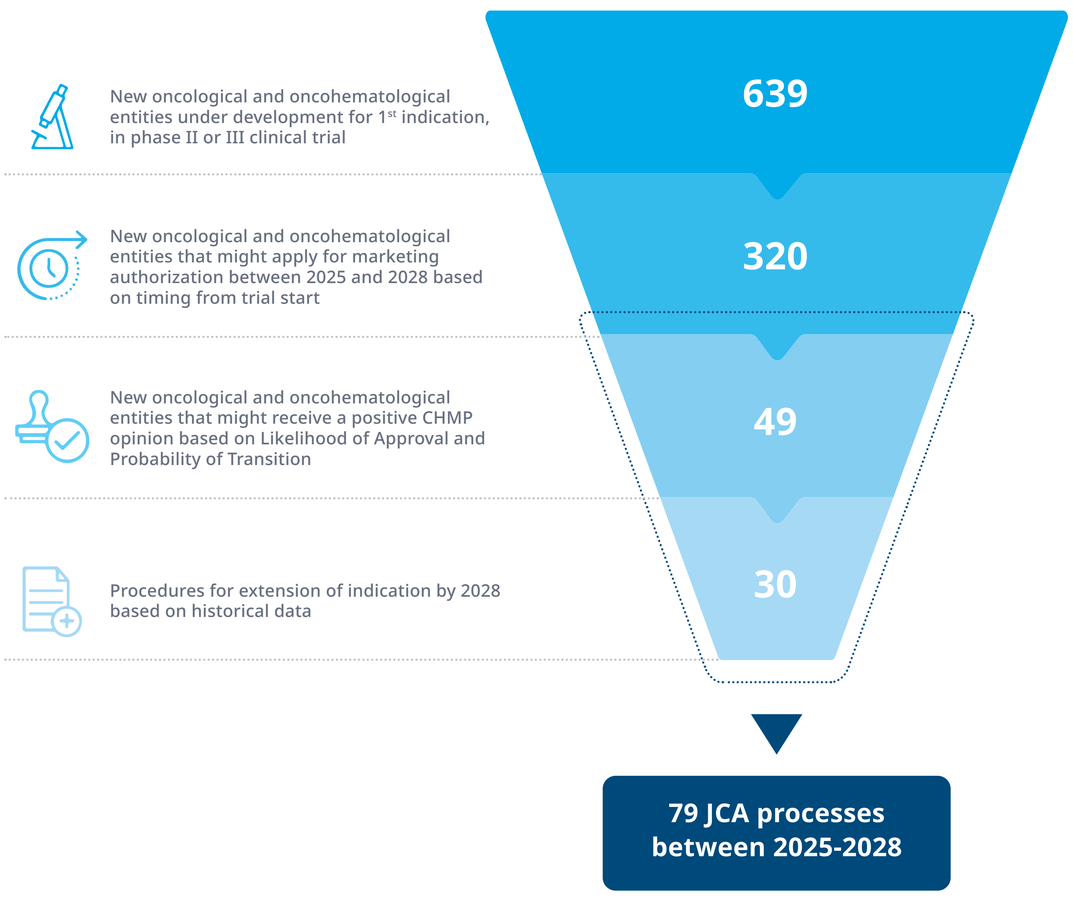


Figure 2. ***Number of estimated JCA processes during the initial phase of HTAR implementation***



Conclusions

Our analysis suggests that during the initial phase of HTAR implementation, 79 JCA procedures will be carried out.

The implementation of the new procedures aims to foster consistent assessment across all Member States gaining efficiency and avoiding duplication.[3] This will be achieved by harmonizing divergent national HTA approaches and establishing standardized methodologies and procedures.[1,2] The novel evaluation criteria introduced by the JCA might also drive changes in local practices concerning evaluation, data collection, evidence generation, and assessment.[3]

It is important to note that our estimates are based on historical data, which provides a solid foundation for our projections. However, the recent surge in R&D investments in oncology could potentially lead to a higher number of approved NTEs, resulting in a rise in JCA procedures undertaken between 2025 and 2028, compared to our estimates.

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