

APPROVAL TIMINGS AND REVIEW SPEED OF IMMUNE CHECKPOINT INHIBITORS (ICIS) IN CANCER THERAPY BETWEEN THE FOOD AND DRUG ADMINISTRATION (FDA) AND THE EUROPEAN MEDICINES AGENCY (EMA) FROM 2010-2022

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Background ICIs targeting cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death protein 1 (PD-1) or its ligand (PD-L1) have transformed outcomes in many cancer types. Prompt regulatory approval is essential to ensure timely access for patients. We have previously shown that over the past decade most new oncology therapies are approved earlier and faster by the FDA compared to the EMA.^{1 2} However, less is known about the regulatory evaluation of ICIs, and if any significant review timing differences exist between initial and subsequent indication approval. In this study, we analyzed regulatory review and approval speed for ICIs at the FDA and EMA following the first ICI approval in 2011.

Methods We performed a cross-sectional analysis of regulatory databases for the FDA and EMA to identify approved ICIs, licensed indications and regulatory review time. ICIs with more than one indication by either the FDA or EMA were included. From each regulatory database we calculated number of approved indications, classified indications by tumor type and calculated the review speed (defined as time from application submission to approval) for each approval. We then compared the regulatory approval timings for initial and supplementary indications (pooled).

Results We identified 8 ICIs, including 7 anti-PD1/PDL1 and 1 anti-CTLA-4 monoclonal antibodies, approved for cancer indications by both the FDA and EMA. There were 93 approved subsequent indications for ICIs, across 14 tumor types with 3 agnostic indications by the FDA with 84 for anti-PD-1/PD-L1, 6 for anti-CTLA4/PD-1 combination therapy and 3 for anti-CTLA-4 monotherapy. This compared to 64 approved indications across 14 tumor types with 1 agnostic indication for the EMA, including 55 anti-PD1/PDL1, 6 for anti-CTLA4/PD-1 combination therapy and 3 for anti-CTLA-4 monotherapy. The median review time for initial ICI approval at the FDA and EMA was 195 days (IQR:172-228 days) and 440 days (IQR: 376-489 days), respectively. For supplementary ICI indication approval, the pooled review time was shorter for each regulator with 180 days (6% shorter) for FDA and 279 days (37% shorter) for the EMA.

Conclusions Eight ICIs have been approved, for similar cancer types, for use in the US and Europe, however, the US has ICIs approved for more indications and agnostic-use labels. ICIs are reviewed more quickly, for both initial and supplementary indications, by the FDA compared to the EMA. Compared to initial approval review, the regulatory review of supplementary indications was relatively unchanged by the FDA but faster by the EMA.

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