**Aim:** Conducting large, well-designed clinical trials for treatments indicated for orphan diseases presents certain challenges, including the low prevalence of such diseases. This study assessed the pivotal clinical evidence package presented in the European public assessment report for orphan-designated treatments with a European Medicines Agency (EMA) marketing authorisation. The evidence packages were compared in terms of the size of patient population in relation to the prevalence of the indicated orphan disease.

**Methods:** All treatments reviewed in this study are assigned to anatomical therapeutic chemical (ATC) category ‘L’. This category was focused on because it is the largest ATC category (contains almost 50% of orphan-designated products) and includes all EMA-approved orphan oncology treatments. All treatments reviewed have been approved within the past 6 years and have been evaluated in a controlled trial using at least one survival-based clinical endpoint. Treatments were compared in terms of patient years (accumulated amount of time that patients are followed up), number of patients in the pivotal trial(s), and disease prevalence (information from Committee for Orphan Medicinal Products public summary of opinion).

**Results:** Fourteen treatments fulfilled the inclusion criteria. Mifamurtide (Mepact®) was an outlier with 4,068 patient years; excluding mifamurtide, patient years ranged from 308 to 2,906 years (median 1,796 years). Mifamurtide was also found to have the second smallest eligible patient population (0.5/10,000 persons). The number of patients in the pivotal trial(s) ranged from 162 to 846 patients (median 485 patients); there were 678 patients in the mifamurtide pivotal trial.

**Conclusions:** The low prevalence of orphan diseases often results in trials with low patient numbers and low patient years. The pivotal evidence package for mifamurtide (indicated for the orphan disease osteosarcoma) has both a small eligible patient population and the largest number of patient years. This study provides support for the robustness of the pivotal evidence package for mifamurtide.

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