The trends in orphan drug authorisation and approval in Europe and in the United States – A retrospective study (2005-2014)
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Background
The definition of an orphan drug (OD) differs depending on where you are in the world and who you are asking. At a high level, an OD may be defined as “a pharmaceutical product aimed at treating rare diseases or disorders”. This definition can be applied across all countries, but there are country-specific differences. However, there are some very close similarities such as the fact that definitions for an OD tend to consider the prevalence of the disease and the estimation of the population affected by the disease.

The definition of a rare disease differs notably between the United States (US) and Europe. In the USA, a rare disease is defined as: <200,000 patients (<9.37 in 10,000), based on US population of 314m in Europe a rare disease is defined as: <5 in 10,000 (<250,000 patients, based on EU population of 506m).

The effect of the variation in definition can be seen clearly by the difference in the number of ODs which have been approved for use by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA).

Since the introduction of the 1983 Orphan Drug Act in the US, there have been over 300 orphan drugs (ODs) approved for use by the FDA. Compare this to the 94 ODs which have been approved for use by the EMA since the adoption of the Orphan Regulation in the European Union (EU) in 2000 (EC201/2000) directive. Since ODs target diseases which have a very high unmet medical need, the regulatory authorities, by using incentives, such as higher price premiums, faster market authorisation and high levels of reimbursement, have made the OD market an attractive market for manufacturers. These incentives have meant that manufacturers have invested in targeted therapies aimed at treating diseases in small patient populations.

A classic example is oncology, which has seen a shift in treatment modalities over the past 20 years from the classical broad-based chemotherapeutic treatment regimes to targeted therapies now used in treating specific cancers in specific subpopulations. For example, last year the FDA approved the use of 13 ODs indicated in oncology.

In this poster, we have studied the number of ODs which have been granted approval or authorisation by the FDA and EMA, respectively, and we have evaluated the trends in designation specifically focusing on the number of ODs which have an indication in oncology.

Methods
- All ODs authorised by the EMA and approved by the US FDA were identified on May 1, 2015 by downloading the databases from the EMA and FDA websites (www.ema.europa.eu/ema and www.accessdata.fda.gov/cumplify/pnp index.jsp) (93 medicines in Europe vs 237 in the US).
- Duplicates were removed in both cases using the non-proprietary name. The lists were then filtered to capture only those medicines that had either received market authorisation (European wording) or market approval (US wording).
- The lists were then filtered again to capture all those medicines that had gained market authorisation or market approval between the period January 1, 2005 to December 31, 2014.
- A summary of the methods used to capture all the ODs authorised or approved for use by the EMA and FDA is shown in figure 1.

Results
In Europe
Two trends can be seen in the number of authorised ODs between the years 2005 and 2014 as outlined in table 1. Firstly, the total number of ODs authorised in 2014 is five times higher than that in 2005 (15 vs 3). Secondly, the number of ODs which have an oncology indication increased over the ten years. Back in 2005, of the total number of ODs authorised that year (three), none of these had an oncology indication. Compare this to 2014, when the total number of ODs authorised that year was 15 and a third of these (five), had an oncology indication. Of the 74 ODs authorised for use in this ten-year time period, 39.2% were included in oncology.

From the United States
Similar trends as shown in the EMA can be seen in the number of ODs approved for use by the FDA between the years 2005 and 2014 as outlined in table 2. The total number of ODs approved for use in this time period more than doubled (14 vs 30) and the number of ODs approved for use with an oncology indication increased more than six times (2 vs 13). Of the 189 ODs approved for use in this ten-year time period, 34.4% of them were included in oncology.

Conclusions
In 2005 the number of ODs authorised was significantly lower than that of 2014, and the designation for orphan diseases and approval of ODs was rare. Ten years on and gaining OD status for a subpopulation-based rare disease appears from the outside to have become an objective for a number of pharmaceutical companies. This can only be a good thing for the patient since the increase in access to medicines treating rare diseases for which before there were no treatment options available will have impacted the lives of these patients positively.

The high numbers of ODs with an oncology indication may be attributed to the exceptionally high unmet need existing in certain cancer subpopulations. The incentives put in place by the regulatory authorities, along with medical advances, will undoubtedly have contributed to the growing trend of targeted cancer therapies which are aimed at treating small subpopulations of patients with specific cancer characteristics. The increasing number of OD authorisations or approvals by the EMA and FDA over the past ten years is evidence that the incentives set by the regulatory authorities to encourage manufacturers to develop treatments for rare diseases has been successful.

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