### Introduction

In July 2006 the Italian Medicines Agency (AIFA) signed the first managed entry agreement (MEA). MEAs are arrangements between manufacturers and payers that enable access to health technologies subject to certain conditions. They have been introduced to manage the uncertainty when patients’ eligibility criteria to treatments are complex and when there is a higher uncertainty on drug’s effects in real-life. These agreements can be divided into two groups: financial agreements, which allow payers to share with the industry the post-marketing budget impact of new drugs and performance-based agreements, that link payers’ commitment to the actual impact of the drugs on health. In Italy both financial-based and performance-based contracts are used: the former includes hidden discounts, cost-sharing, spending caps and price/volume agreements; the latter includes performance-linked reimbursement contracts, which limit reimbursement to patients responding to the treatment (payment by result, risk-sharing or success fee). Cost-sharing, payment by result and risk-sharing rely on monitoring registries implemented by AIFA, which allow to track each single patient in the real world setting and collect data needed for the purpose of the agreement. In Italy, as well as in other healthcare systems, MEAs conditions and negotiated price discounts are confidential.

### Results

In the considered timeframe, the number of Registries increased significantly (+99%), from 90 Registries in 2013 to 179 in 2018 (including 16 web-based Therapeutic Plans (TP)). A similar trend can be observed by looking at the number of patients (from 149,447 in 2013 to 1,958 MIO in 2018) and treatments (from 143,012 in 2013 to 2,204 MIO in 2018).

### Methods

A review of the existing MEAs has been performed by checking all the available data on Registries active in September 2019 and the information coming from the annual reports released by the Osservatorio Nazionale per l’Impiego dei Medicinali (Osmed) and published between 2013 and 2018.

### Conclusions

Starting from 2013 the number of MEAs and registries linked to them has increased considerably. On the other hand, the number of performance-based schemes agreed and applied had been decreasing significantly year by year until their complete disappearance in 2017-2018. This may be related to the complexity associated with these tools, starting from the difficulty to define the patient’s responsiveness to the administrative burden of their practical management. Nevertheless, as demonstrated by the numbers, MEAs positive impact in terms of savings is unquestionable.

The arrival of the costly cell and gene therapies, one-shot administered, with a long life efficacy, will probably lead to a new era for these negotiating tools. Recently AIFA has officially declared a successful agreement between its pricing and reimbursement committee (CPR) and Novartis for reimbursement of the CAR-T cell therapy Kymriah, by relaxing some details, such as the adoption of a split payment scheme (already applied for the first time to Sirivoltis) and a payment by result reimbursement model. Payment of the drug will be done in three instalments (at the time of infusion, after six months and after 12 months); if AIFA records show that treatment is unsuccessful at any point in the 12-month period, hospitals will not have to make any subsequent payments.

It will be extremely interesting to observe the future development of such ‘relooked’ performance-based schemes, which role could be interesting in granting access to new coming innovative technologies.