Conditional agreements for innovative therapies in Italy: the case of Pirfenidone

Fasci A1, Ferrario M1, Ravasio R2, Ena R1, Angelini S1, Giuliani G3
1Hoffmann-La Roche, Monza, Italy, 2Health Publishing & Services, Milano, Italy, 3Roche SpA, Monza, Italy

Background

In 2005, AIFA (Italian Drug Agency) implemented drug registries to ensure appropriate use of the treatment and enabling conditional agreements (i.e., risk-sharing) until the risk/benefit ratio of the drug is confirmed in clinical practice.

Strong collaboration between AIFA, Clinicians, Hospital Pharmacists, Pharmacologists, Payers (Regional and Local) and pharmaceutical companies is needed through the Registers management (i.e., prescription, purchasing process, effectiveness evaluation).

Registries permit to collect real world data to re-assess the clinical value in clinical practice (i.e., effectiveness) enabling a value-based pricing approach.

For all stakeholders, registries represent an opportunity to work together in the light of partnership.

3. Nathan Registry warranted development of new diagnostic tests as well as new treatments.

Data from AIFA Registers for reassessment of innovative therapies

Material and methods

Web-based AIFA Registry is a Web-based tool, created by AIFA on a drug specific bases, allowing:

- Clinicians to register patients ensuring the eligibility of the patient and his monitoring;
- Hospital pharmacist to dispense the drug within NHS funds;
- AIFA to collect data to evaluate drug effectiveness in real practice
- Companies to manage innovative pricing schemes (i.e. cost-sharing, payment by results)

Risk sharing agreement based upon CAPACITY trial study results was the result of the first negotiation in 2013.

- Based on the agreement, patients presenting a FVC≥10% decline at 6 month follow up (i.e., decline of 10 percentage calculated as delta from day 0 of therapy) were not allowed to continue the treatment with pirfenidone and initial 6 months were paid by the company.

Results

Registry warranted pirfenidone the appropriate use in line with the eligibility criteria of clinical trials allowing higher adherence and persistence rates than EU values (80%ITA vs. 72%EU and 73%ITA vs. 50%EU, respectively).1

New Phase III RCT data2 and clinical practice3 data strengthening pirfenidone value were submitted for the re-negotiation to reassess the cost-benefit profile:

1. Data from ASCEND study shows:
   - Treatment with pirfenidone significantly reduced disease progression, as measured by changes in % predicted FVC (p=0.000001) (Fig. 1).
   - Changes in 6-minute walk distance (p=0.036).
   - Treatment with pirfenidone reduced all-cause mortality in a pre-specified pooled analyses at week 52 (p=0.011).

2. Pre-specified pooled analysis of data from CAPACITY and ASCEND studies demonstrate that even patients experiencing ≥10% FVC decline in the first 6 months benefit from treatment continuation (Fig. 2).

3. Data form a RWE4 cohort of patients confirmed effectiveness of pirfenidone:
   - Largest real life data cohort (n=197) of pirfenidone in IPF.
   - Includes 113 patients from Turin University Clinic.
   - Endpoints: Analysis of change of FVC before and after start of treatment with pirfenidone (Fig. 3):
     - FVC decline before treatment: -7.0 ± 1.8% (-248.1 ± 199.3 ml per year)
     - FVC decline with Pirfenidone therapy: +2.6 ± 3.6% (+514 ± 351.4 ml per year) (p=0.0001)

4. Data from AIFA Registry effectiveness and tolerability were positively perceived during the renegotiation.

- Thanks to these evidences, the uncertainty around the benefit in clinical practice was overcome; AIFA agreed to withdraw the risk-sharing: the drug is still available in AIFA Registry to monitor the appropriateness of use. As a result:
  - Stopping rules were removed from the registry (Fig. 4).
  - Drug effectiveness continue to be collected through registry to consolidate information to define product value.

Conclusions

When the risk/benefit ratio is not yet been sufficiently defined, this approach allows to reduce uncertainties and to re-assess health technologies in line with health policies.

At present AIFA negotiated with Pharmaceutical companies more than 120 registries.

It is expected that in the future there will be an increased use of data collected through AIFA Registers for reassessment of innovative therapies.

References:

1. Roche data on file.

Discussion

Data collected through AIFA registries supplemented with ASCEND data and RWE data allow both Agency and Company to re-assess pirfenidone value.

Pre specified ASCEND pooled Analysis and Pooled data from registry allow to understand that FVC≥10% decline within 6 month is not a direct proxy of drug effectiveness.