Poster Code: HPR24

CRITICAL ANALYSIS ON TIME-TO-REIMBURSEMENT OF RARE DISEASE DRUGS: THE ITALIAN CASE (AIFA Commissions 2018 - 2022)

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BACKGROUND AND OBJECTIVE

Market Access for pharmaceuticals in Italy is regulated by the Italian Medicines Agency (AIFA): rapid and equal access to new treatments represents the final goal for the National Health Service (NHS), in order to guarantee innovative therapies to a wider range of patients. In the context of Rare diseases – where therapeutic alternatives are limited and unmet medical need clearly high – a faster access should be desirable. Conventional appraisal methods may be unsuitable for assessing the value of rare disease treatments, thus leading to possible delay in Time to Reimbursement (TtR). The following analysis aims at identifying potential key factors influencing TtR of Rare disease Drugs (RD) versus Non-Rare disease Drugs (NRD) in Italy throughout the evaluation of AIFA Scientific Technical Committee (CTS) and Price Reimbursement Committee (CPR) assessment process.

MATERIALS AND METHODS

We query the MA Provider database to identify drugs evaluated and reimbursed in Italy – upon EMA centralized authorization – during the period of the current AIFA commissions (October 2018 to April 2022): for drugs that started the evaluation process under the current commissions and concluded the process over the period identified, information related to TtR and procedural steps taken to reach the agreement have been collected **(Figure 1)**. The total duration of reimbursement process (from dossier submission to publication in the Official Journal) and the time for single assessment phases have been measured **(Figure 2)**; to minimize the possible impact of outliers, results values are presented as median values. The primary analysis was performed on the entire sample, by comparing RD vs. NRD, while orphan designation and innovative status (granted by AIFA) were evaluated as subanalyses. The number of CTS/CPR postponed procedures and investigations was examined as a potential factor influencing the process.

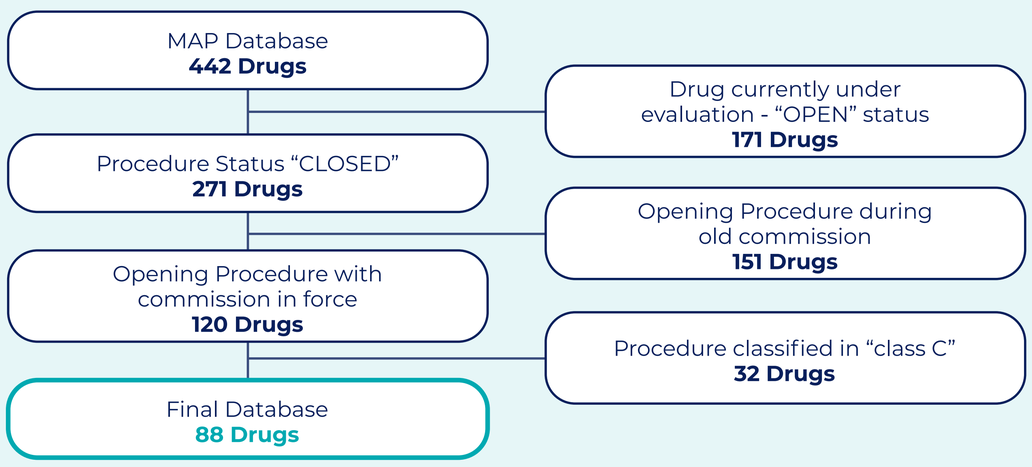


Figure 1. MAP database: definition of final sample for analysis

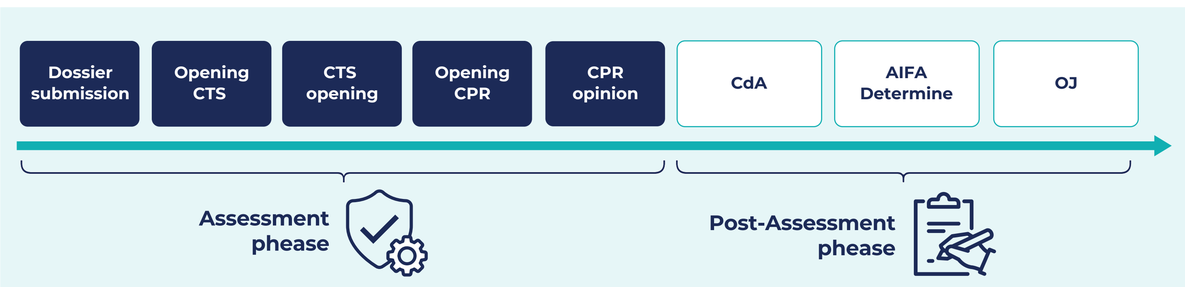


Figure 2. Procedural steps along the AIFA assessment process

RESULTS

88 drugs (39 RD vs 49 NRD) completed the P&R process within the identified temporal window and were included in the analysis: the total median duration of P&R process was 438.0 days.
The total duration of P&R process for RD was 74.0 days longer compared to NRD (479.0 for RD vs. 405.0 days for NRD) **(Figure 3)**. The breakdown analysis for single steps pointed out that CTS assessment (70.0 for RD vs. 33.0 days for NRD) and CRP assessment (122.0 for RD vs 97.0 days for NRD) were 37.0 days and 25.0 days longer, respectively. Among RD, 74% (29/39) were orphan drugs. Orphan designation seems to correlate with a lengthening in the total assessment period (493.0 for orphan RD vs. 396.5 days for non-orphan RD): of notice, orphan RD spends +68.5 and +135.5 days for CTS and CPR assessment, respectively **(Figure 4)**.
Preliminary analyses on the role of innovative status showed a possible positive correlation between TtR and innovativeness: for orphan RD, we reported 456.0 days for innovative orphan RD vs. 522.5 days for non-innovative orphan RD; despite a less pronounced difference, the trend was maintained also for NRD (403.5 for innovative NRD vs. 426.0 days for non-innovative NRD).
Overall, RD and in particular orphan RD reported the longest TtR, which according to our analyses, may be ascribed to the increased number of CTS/CPR investigations and CPR hearings rather than to the number of postponed procedures **(Figure 5)**

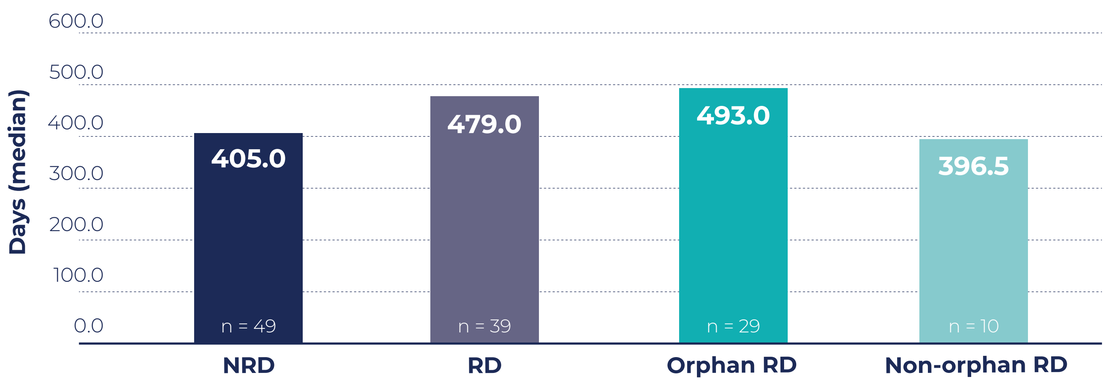
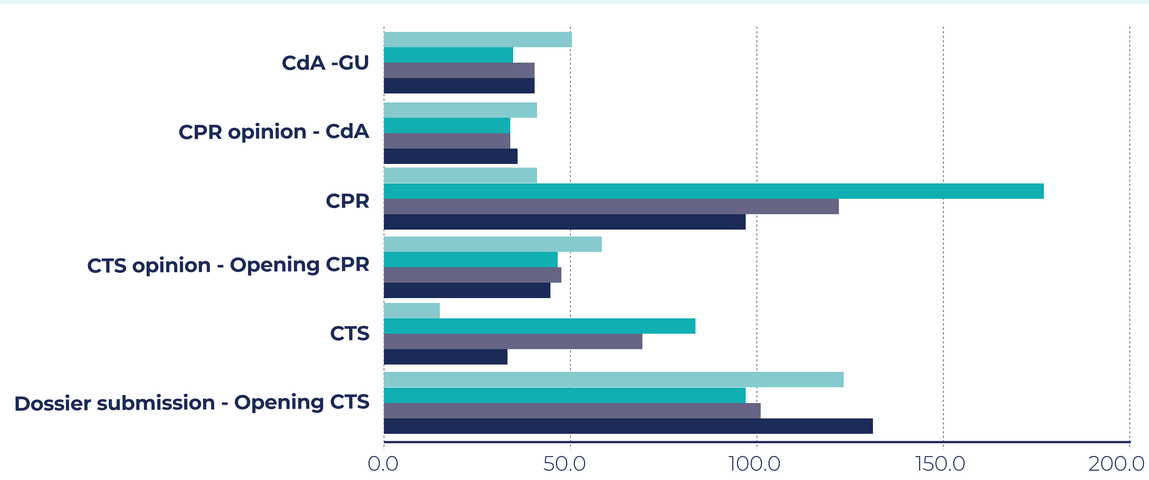


Figure 3. Comparative analysis of TtR: focus on RD vs. NRD and orphan designation



	Dossier submission - Opening CTS	CTS	CTS opinion - Opening CRP	CPR	CTS opinion - CdA	CdA -GU
Non orphan RD	124.0	15.5	58.5	41.5	41.5	51.0
Orphan RD	97.0	84.0	47.0	117.0	34.0	35.0
RD	101.0	70.0	48.0	122.0	34.0	41.0
NRD	131.0	33.0	45.0	97.0	36.0	41.0

Figure 4. Procedural steps analysis across pre-specified group

A	CTS investigations	CTS hearing	CTS postponed procedures	CPR investigations	CPR hearing	CPR postponed procedures
RD (n=39)	**2.0** (0 - 6.0)	**0.0** (0 - 1.0)	**0.0** (0 - 3.0)	**3.0** (0 - 7.0)	**1.0** (0 - 4.0)	**0.0** (0 - 2.0)
NRD (n=49)	**1.0** (0 - 8.0)	**0.0** (0 - 2.0)	**0.0** (0 - 3.0)	**2.0** (0 - 10.0)	**0.0** (0 - 2.0)	**0.0** (0 - 3.0)
Orphan RD (n=29)	**2.0** (0 - 6.0)	**0.0** (0 - 1.0)	**0.0** (0 - 3.0)	**3.0** (1 - 7.0)	**1.0** (0 - 4.0)	**0.0** (0 - 2.0)
Non orphan RD (n=10)	**0.5** (0 - 3.0)	**0.0** (0 - 1.0)	**0.0** (0 - 2.0)	**2.5** (0 - 5.0)	**0.0** (0 - 1.0)	**0.0** (0 - 1.0)

Figure 5. Focus on CTS and CPR (values shown as median [min – max])

CONCLUSIONS

Combining innovation and sustainability, through the evaluation of the therapeutic efficacy and cost-benefit of new medicines, is a major challenge for AIFA. With respect to rare disease – where available therapeutics alternative are limited – a faster P&R process may be crucial to guarantee innovative therapies to patients. Our analysis indicates that TtR for RD is longer compared to NRD; additionally, for orphan RD, TtR is even longer. The delay in the approval process can be ascribed to the increased number of CTS/CPR investigations, that AIFA considered necessary to validate the quality of evidence and mitigate the possible uncertainties related to the number of patients to treat and proposed price. We strongly believe that improving the efficiency of the assessment process while reducing TtR will be crucial to enhance market penetration of drugs for rare disease patients.

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