Assessing COA Label Claims Based on Single-arm Trials in Rare Diseases: A Review of US FDA Labels

Divyesh Thakker[1], Hugo Dubucq[2], Sylvie Bozzi[3], Benoit Arnould[3], Juan-Guillermo Jasso-Mosqueda[3]

[1]Sanofi, Hyderabad, Telangana, India; [2]Sanofi, Barcelona, Spain; [3]Sanofi, Chilly-Mazarin, Paris, France

Poster Number: HPR12

Introduction

- A clinical outcome assessment (COA) is a measure that describes or reflects how a patient feels, functions, or survives. Patient-reported outcome (PRO) is a type of COA.
- The United States Food and Drug Administration (US-FDA) PRO guidance published in 2009 defines PRO instrument, as a tool to collect PRO data to assess treatment benefit or risk in the clinical trials of medical products.[1]
- PRO data assessment is used to support the claims in approved medical product labelling.
- PRO serves as a crucial criterion for patients with chronic diseases; it is very helpful to have a label claim say that some aspect of quality of life has improved.
- The US-FDA lists various requirements for label claims and one of the study design requirements for PRO labelling claims is a randomised, blinded, clinical trial.
- However, in the context of rare diseases (RDs), registration trials are frequently conducted without a comparator arm.[2]

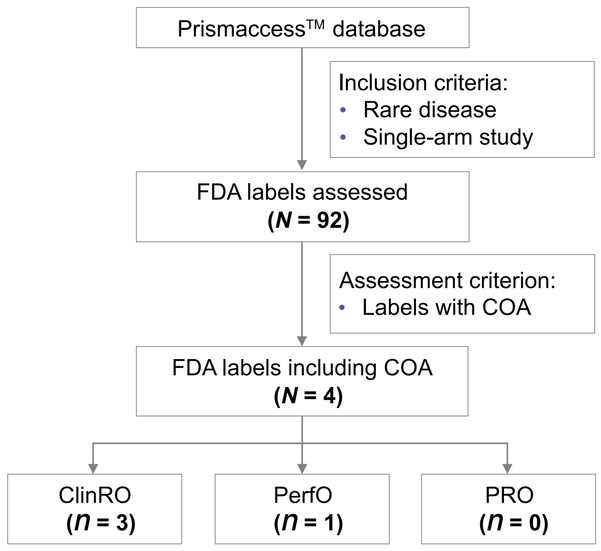
Objectives

- The aim of the current review was to assess experience of COA/PRO with regards to label claims, using single-arm studies in the RD area.

Methodology

- The US FDA labels considering single-arm trials in the RD area were identified through the Prismaccess™ platform (IQVIA) from inception (**Figure 1**).
- PRO is one of the COA tools – along with observer-reported outcomes (ObsROs), clinician-reported outcomes (ClinROs), and performance outcomes (PerfOs).
- **Table 1** represents glossary of types of COA.
- Labels were reviewed to identify whether a COA label claim was granted for these molecules based on the single-arm studies (**Figure 1**).
- For labels including COA, the outcome was further categorised as a ClinRO, PRO, or PerfO (**Figure 1**).
- For these labels, the 'Indications and Usage' section as well as the 'Section 14 Clinical Studies' of each label were examined, and categorised based on following:
  a. Whether a COA was included in the study (yes/no)?
     i. Is it a ClinRO (yes/no)?
     ii. Is it a PRO (yes/no)?
     iii. Is it a PerfO (yes/no)?
- The assessment of these label sections determined whether a COA/PRO label claim was granted for these molecules.

Figure 1. Selection of labels.



COA, Clinical outcome assessment; ClinRO, Clinician-reported outcome measures; FDA, Food and Drug Administration; PerfO, Performance outcome measures; PRO, Patient-reported outcome measures

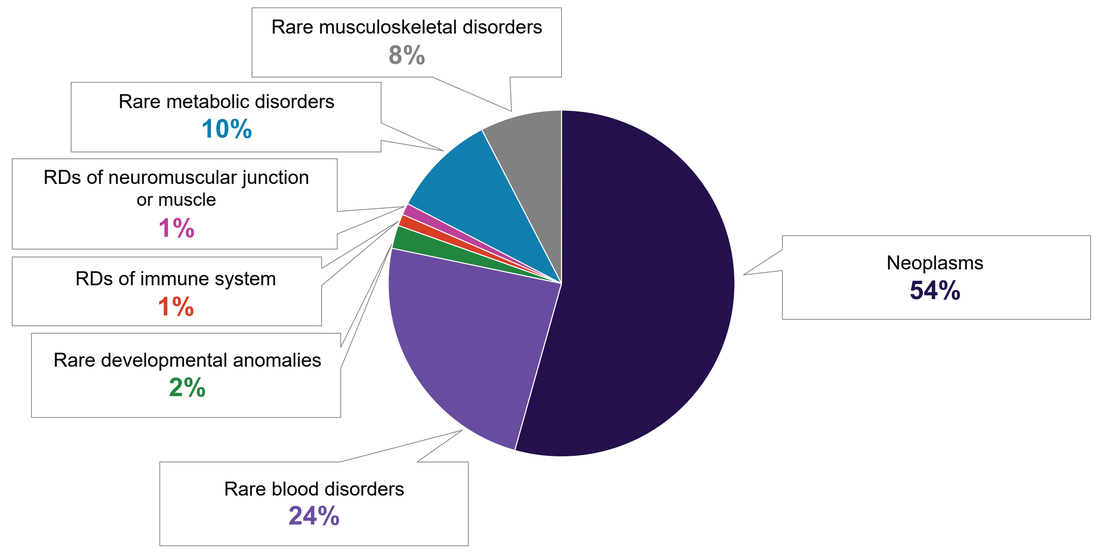
Table 1. Types of Clinical Outcome Assessments (COAs).[3]

Types of COA	Definition	Rating scales
Patient-reported outcome measures	A measurement based on a report that comes directly from the patient (i.e., study subject) about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else. It captures patient's own evaluation of the impact of a disease and/or treatment on their quality of life, daily function, or symptoms.	• Rating scales (e.g., numeric rating scale of pain intensity or Minnesota Living with Heart Failure Questionnaire for assessing heart failure) • Counts of events (e.g., patient-completed log of emesis episodes or micturition episodes)
Observer-reported outcome measures	A measurement based on a report of observable signs, events or behaviours related to a patient's health condition by someone other than the patient or a health professional.	Rating scales, such as: • Acute Otitis Media Severity of Symptoms scale (AOM-SOS), a measure used to assess signs and behaviours related to acute otitis media in infants • Face, Legs, Activity, Cry, Consolability scale (FLACC), a measure used to assess signs and behaviors related to pain • Counts of events (e.g., observer-completed log of seizure episodes)
Clinician-reported outcome measures	A measurement based on a report that comes from a trained health-care professional after observation of a patient's health condition.	Rating scales, such as: • Psoriasis Area and Severity Index (PASI) for measurement of severity and extent of a patient's psoriasis • Hamilton Depression Rating Scale (HAM-D) for assessment of depression
Performance outcome measures	A measurement based on standardised task(s) actively undertaken by a patient according to a set of instructions.	• Measures of gait speed (e.g., timed 25-foot walk test using a stopwatch or using sensors on ankles) • Measures of memory (e.g., word recall test)

Results

- As of April 6, 2023, a total of 92 FDA labels for molecules that had FDA submissions based on single-arm studies in the RD field were found in the Prismaccess™ database (**Figure 2**).
- Only four out of 92 labels included COA; three were ClinRO and one was PerfO (**Table 2**).
- None of the retrieved labels included PRO.
- The US FDA did not grant any PRO label claim, however, in exceptional cases, ClinRO or PerfO label claim were awarded to products that underwent submission based on single-arm trials in RD.

Figure 2. Distribution of retrieved labels among RD areas (*N* = 92).



RD, rare disease

Table 2. Characteristics of FDA label claim for rare indications with COA.

Drug name	International nonproprietary name	Therapeutic area	Indication	List of reported endpoints	COA (yes/no)	ClinRO (yes/no)	PRO (yes/no)	PerfO (yes/no)
SKYSONA	Elivaldogene autotemcel	Gene Therapy in Cerebral Adrenoleukodystrophy (CALD)	Indicated to slow the progression of neurologic dysfunction in boys 4–17 years of age with early, active CALD	Neurologic function scores Major Functional Disability (MFD)-free Survival	Yes	Yes	No	No
EVRYSDI	Risdiplam	Spinal muscular atrophy (SMA)	Indicated for the treatment of SMA in paediatric and adult patients	Part 2 study was RCT Motor Function and Development Milestones: Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III), Item 22: sitting without support for at least 5 seconds Survival and Event-Free Survival: Alive without Permanent Ventilation	Yes	No	No	Yes
BRINEURA	Cerliponase alfa	Neuronal ceroid lipofuscinosis	Indicated to slow the loss of ambulation in symptomatic paediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 deficiency	Decline in the Motor domain of the CLN2 Clinical Rating Scale	Yes	Yes	No	Yes
ORENCIA	Abatacept	Juvenile idiopathic arthritis (JIA) Polyarticular JIA (pJIA)	Indicated for moderately to severely active pJIA in paediatric patients 2 years of age and older. It may be used as monotherapy or concomitantly with methotrexate	Study JIA-1 (Period A only, period B is RCT): ACR 30/50/70 responses Study JIA-2: ACR 30/50/70 responses	Yes	Yes	No	No

ACR, American college of rheumatology; ClinRO, Clinician-reported; ObsRO, Observer-reported; PRO, Patient reported; Perfo, Performance outcome; RCT, Randomised clinical trial.

Conclusions

- None of the molecules with single-arm trial data was granted a PRO label claim in RD area.
- In the RD area where non-conventional study design is accepted by regulatory bodies, it would be important to increase the recognition of ClinRO, PerfO and PRO label claims in order to better inform prescribers and patients about clinical benefits expected from innovative treatments.

REFERENCES

1. U.S. Food and Drug Administration. Guidance for industry patient-reported outcome measures: use in medical product development to support labeling claims; 2009. Accessed on: 20 September 2023.
2. Selaru P et al. *Clin Transl Sci*. 2016;9(2):63–73.
3. U.S. Food and Drug Administration. Clinical Outcome Assessment (COA): frequently asked questions. Available at:https://www.fda.gov/about-fda/clinical-outcome-assessment-coa-frequently-asked-questions#:~:text=A%20clinical%20outcome%20assessment%20is,%2Dreported%20outcome%20(ObsRO)%20measures. Accessed on: 20 September 2023.

FUNDING

This study was funded by Sanofi.

ACKNOWLEDGEMENT

Medical writing support was provided by Aayushi Ambastha and Deepshikha Roy from Sanofi.

CONFLICT OF INTERESTS

DT, HD, SB, BA, and **JGJM** are employees of Sanofi and hold stock or stock options of Sanofi.

International Society for Pharmacoeconomics and Outcomes Research (ISPOR)-EU 2023 (November 12–15, 2023), Copenhagen, Denmark