Novel Patient-Centered Approach to Clinical Trial Readiness in Rare Diseases

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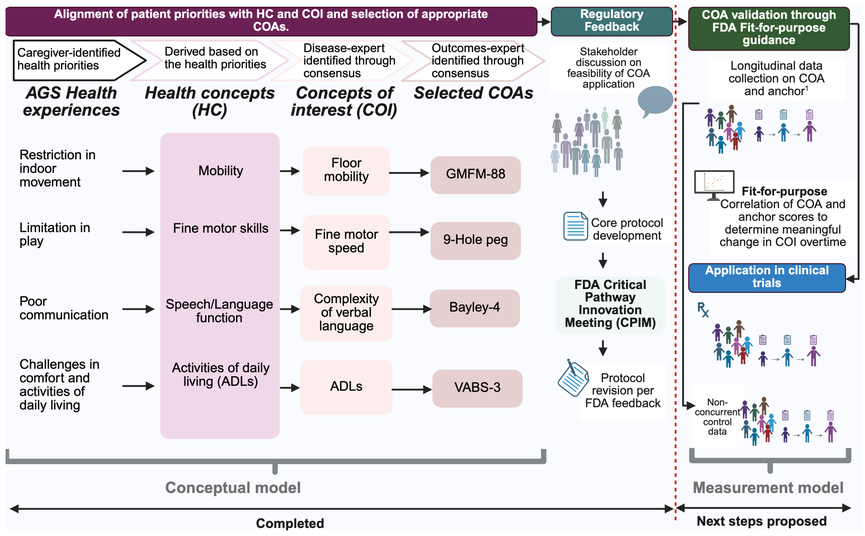
BACKGROUND

Figure 1: The 2022 Food and Drug Administration (FDA) four-part guidance on Patient-Focused Drug Development (PFDD)



OBJECTIVE: We propose a novel multi-component sequential approach to designing a Patient-centered Clinical Outcome Assessment (COA) protocol for rare disease clinical trials and pilot in Aicardi-Goutières Syndrome.

APPROACH

STEP 1: Identification of caregiver priorities (HCs)

- Patient/caregivers completed qualitative interviews and REDCap-based Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD) survey.

STEP 2: Identification of fit-for-purpose COIs

- Consensus-building approach among disease experts,
- *"Important"* and *"Changeable (within 12 months of intervention)"* in the context of a clinical trial.

STEP 3: Selection of COAs

- Consensus building among specialty-specific subpanels on *"measurability"* and *"reproducibility"* of the COAs.
- Group discussion sandwiched between pre- and post- focus group surveys for each sub-panel.

STEP 4: Patient/Caregiver stakeholder feedback

- Assess the feasibility of COA completion.

RESULTS

Table 1: Identification of patient priorities (HCs), alignment with fit-for-purpose COIs, and selection of appropriate COAs

Health Concepts	Concepts of Interest (COIs)	Clinical Outcome Assessments (COAs)
Clinician Reported Outcome		
Mobility	Postural Function (head and trunk) Neurologic dysfunction	AGS Severity Scale
Communication/Social	Complexity of verbal language	Denver Developmental Scale -2nd edition
Overall health and comfort	Skin lesions	Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index (RCLASI)
Performance Outcome		
Communication	Preferential looking	Eye tracker (Preferential Looking Protocols)
Mobility	Postural Function Floor mobility Neurologic dysfunction	Hammersmith Infant Neurologic Examination (HINE)
Fine motor	Fine motor speed	9-Hole peg
Communication/Social **Mobility**	Complexity of verbal language Postural Function (head and trunk) Floor mobility	Bayley Scales of Infant and Toddler Development- 4th edition
Fine motor	Fine motor speed	Developmental Neuropsychological Assessment- 2nd edition (NEPSY-II)
Communication/Social **Mobility**	Complexity of verbal language Postural Function (head and trunk) Floor mobility	Leiter-3
Mobility	Fatiguability (Endurance) in completion of motor tasks	6 Minute Walk Test (6MWT)
Mobility	Floor mobility Postural Function (head and trunk)	Gross Motor Function Measure-88 (GMFM-88)
Mobility	Floor mobility	Wearables*
Observer Reported/Patient Reported Outcome		
Communication/Social **Activities of Daily Living**	Communication through behavior Complexity of verbal language Imitation of activities Independence in completion of activities of daily living	Vineland Adaptive Behavior Scale- 3rd edition
Activities of Daily Living	Independence in completion of activities of daily living	Pediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDICAT)

Figure 2: Stakeholder feedback and incorporation into protocol

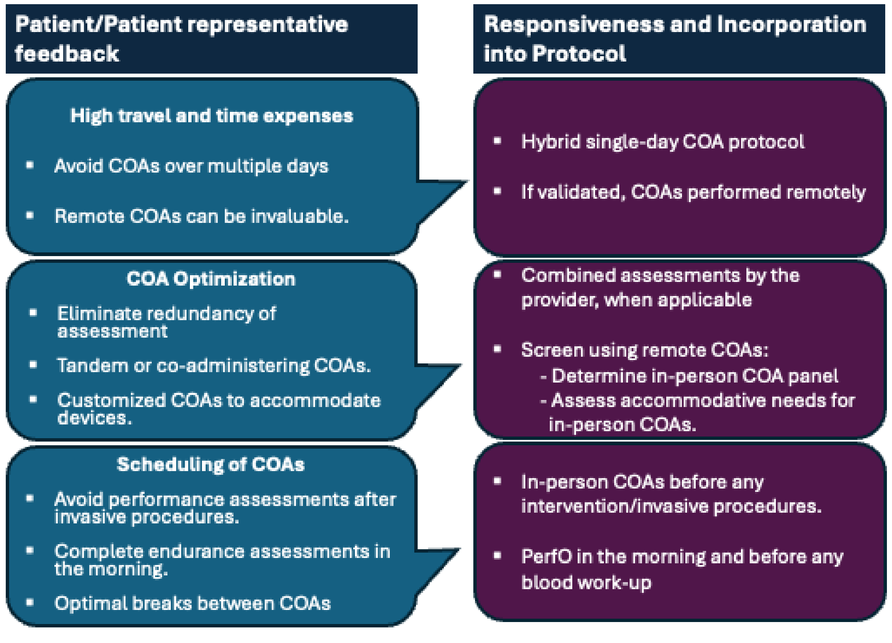
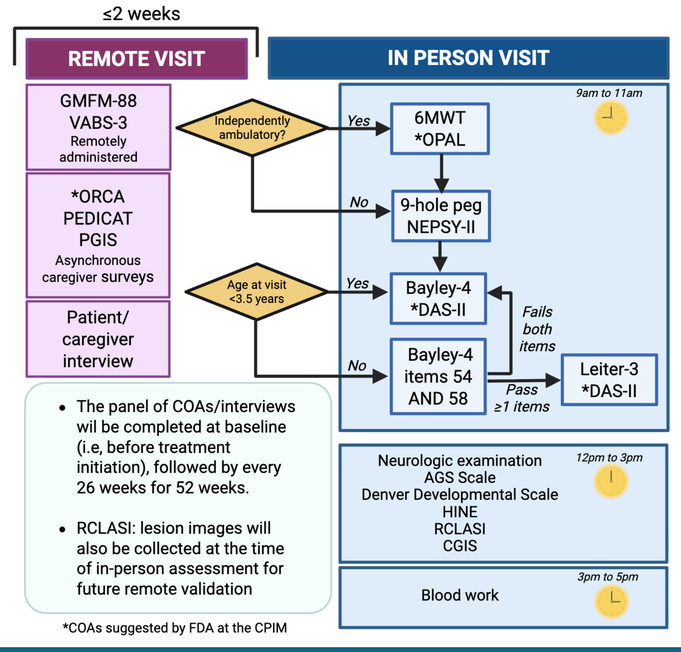


Figure 3: Patient-Centered Core COA protocol



CONCLUSION

FDA's PFDD-aligned approach that yields a <u>shareable fit-for-purpose toolkit</u> of COI-COA panel and a disease-specific protocol for rare disease drug development.

- By incorporating patient/caregiver perspectives and lived experiences at early stages, the approach embeds patient-centricity at the core of rare disease clinical trial design.
- Protocol application in a prospective study will yield a rigorous longitudinal COA data applicable as a control cohort for future clinical trials.