PATIENT FOCUSED DRUG DEVELOPMENT FOR PML

Considerations for PML Clinical Trial Designs

Joan Ohayon
MSN, CRNP, MSCN
NINDS

September 21, 2021

PATIENT-FOCUSED DRUG DEVELOPMENT

- Systematic approach to help ensure that patients' **experiences, perspectives, needs, and priorities** are captured and meaningfully incorporated into drug development and evaluation

- Patients are uniquely positioned to inform the understanding of the therapeutic context for drug development and evaluation

OBTAINING THE PATIENTS' VOICE: OBSTACLES WITH PML

- High mortality and rapid disease progression
- Survival:
  - HIV 50% - 2 years
  - MS 77% - 3 years
  - Hematologic malignancies 10% - 2 months
- Delays in diagnosis
- Neurologic impairment (affecting mobility, mentation, speech)

OUR INITIATIVES:

Patient Listening Sessions *(July 22 and September 11, 2020)*:

- Collaborated with FDA Office of Patient Affairs (OPA)
- Conducted 2 PML Patient Listening Sessions (PLS)
  - Small, informal, non-regulatory, non-public discussions about disease experiences, not a specific medical product, that are of interest to FDA medical staff

External Crowdsourcing Pilot *(July 2021)*:

- Collaborated with FDA Office of Patient Affairs & FDA/CDER Office of Strategic Programs
- Initiated external crowdsourcing
  - Web-based platform providing opportunities for patients/caregivers to engage with each other and share experiences – with the guidance of moderators from FDA

PATIENT LISTENING SESSIONS

- Developed questions for survey to elicit thoughts, opinions and perspectives of the patients and caregivers on the challenges of living and coping with PML
- Identified a subgroup of PML patients and their caregivers representing the diverse spectrum of perspectives
- Conducted 90 min sessions asking questions to all participants regarding their experiences with PML; FDA/NIH participated as listeners to gain insight
- Summaries available at: https://www.fda.gov/patients/learn-about-fda-patient-engagement/patient-listening-session-summaries

PLS PARTICIPANTS

Patient vs Caregiver:

- 5 -PML pts: 3 dx 1 - 5 years ago; 2 dx 5-10 years ago
- 12 – caregivers: 4 cared for pts dx in past year; 6 cared for pts dx 1-5 years ago; 2 cared for pts dx 5 - 10 years ago

PML Survival: 5 of the PML pts represented had died

Underlying disease experience:

- HIV (1 pt, 1 caregiver)
- MS (3 pts, 1 caregiver)
- PIDD (1 caregiver)
- Hematologic malignancy (1 patient, 6 caregivers)
- ICL (1 caregiver)
- Sarcoidosis (1 caregiver)
- Autoimmune (1 caregiver)

EXTERNAL CROWDSOURCING FOR **PATIENT-FOCUSED DRUG DEVELOPMENT**

Provided an opportunity for individuals with PML and their loved ones to **share experiences**.

Demonstrated platform's ability to function as a **"listening" mechanism** for CDER.

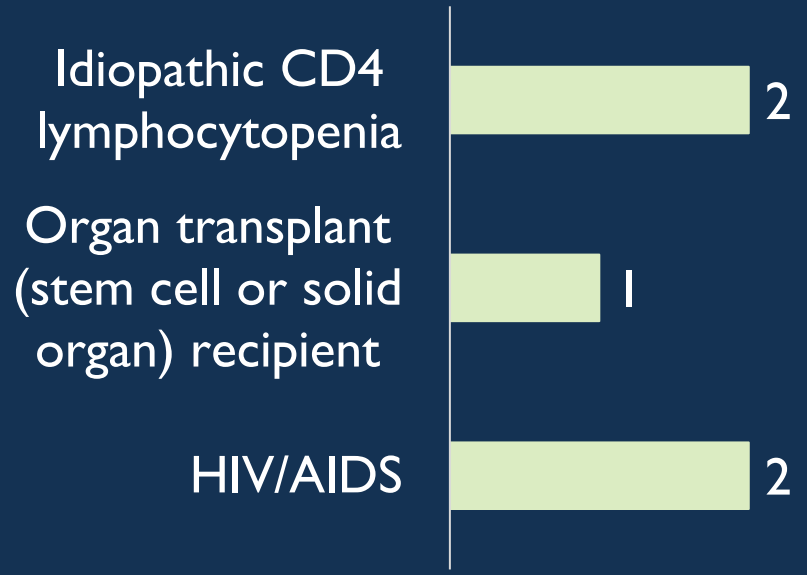
Answers to core questions related to daily life, treatment approach, and patient concerns are shared at this FDA PML Clinical Trial Design Workshop and will be included in an internal PML Patient Focused Drug Development report and/or in a manuscript summarizing the information learned through the patient experience.

EXTERNAL CROWDSOURCING PARTICIPATION:

There were **5 submissions** during this initiative. Four of those who posted were caregivers/family.

Submitters (caregivers/family and patients) identified with **all PML diagnosis date categories**.

Submitters (caregivers/family and patients) identified with **3 of the 7 underlying conditions** listed in the form.*



*No submitters selected the options "None of the above" or "Other" for underlying conditions.

BARRIERS FOR CLINICAL TRIAL PARTICIPATION FOR PML PATIENT

- Lack of knowledge of studies
- Lack of availability of studies
- Rapid disease progression/mortality
- Painful procedures
- Onerous tests (i.e. frequent LPs)
- Ineligibility due to tx hx
- Limitations in mobility
- Challenges of travel, family responsibilities, finances
- Challenges of neurological manifestations of PML
- Delayed diagnoses

> 50% expressed uneasiness with placebo-controlled trials for PML

- Believed placebo would waste valuable time and would defeat the purpose of treatment
- Expressed understanding the necessity for the placebo but would choose not to participate

A few would have taken any opportunity:

- To delay, reverse, or stop progression of symptoms, including participating in a trial with a placebo
- Placebo better than no option

MOTIVATIONS:

- Access to PML experts
- Access to early diagnosis
- Increasing knowledge
- Limited options
- Desire to contribute

SUMMARY

- PLS demonstrated that it is possible to elicit the PML patient voice to inform PML clinical trial design considerations
- External crowdsourcing showed similar themes to PLS re barriers/motivators among participants
- PML patients and their caregivers are willing to share their perspectives even when doing so is challenging emotionally

*High mortality and **rapid** progression*

Neurological symptoms – burden on patient/caregiver

Challenges of travel, family responsibilities, finances

Balancing expectations

Quality of life

MOVING FORWARD WITH CLINICAL TRIAL DEVELOPMENT:

- Integrating the PML patient voice into PML clinical trial development will be essential to clinical trial recruitment and retention.
- Clinical trialists and product sponsors should refer to FDA guidance on patient focused drug development. https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical

ACKNOWLEDGEMENTS

- PML patients and caregivers:
    - FDA Patient Listening Session participants
    - FDA External Crowdsourcing participants
- FDA Office of Patient Affairs
- FDA/CDER Office of Strategic Programs
- National Organization for Rare Disorders
- PML Patient Focused Drug Development Working Group Members
- FDA/CDER, FDA/CBER, and NIH
- Referring clinicians