Assessment of Effectiveness in Clinical Trials

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Clinical Evidence

Effectiveness evaluation – clinician reported outcomes (ClinROs)

- Validated sponsor-specific scale assesses wrinkle and/or defect severity from a clinician's perspective for the proposed indication for use
- Typically a 4 or 5 grade photonumeric scale that is validated to demonstrate good intra- and inter-rater agreement
- Validated to demonstrate the ability of a change on the scale to represent a clinically meaningful change
- Validated using photographs or through live validation

Clinical Evidence

Effectiveness evaluation challenges – ClinROs

- Some scales are proprietary, developed and validated by the sponsor of the clinical study
- A review of effectiveness scales used to evaluate the nasolabial folds showed that out of 13 different PMAs, 7 different effectiveness scales were used
  - Live and photo evaluation
  - Primary effectiveness endpoint evaluations performed at various timepoints ranging from 12 weeks to 13 months after treatment
- Results of clinical studies are challenging to compare

Clinical Evidence

Effectiveness evaluation challenges – patient reported outcomes (PRO)

- Studies typically include input from the patient as secondary or ancillary effectiveness endpoints
- Validated patient-reported outcomes (PROs) assessed by subjects throughout the study
- Study sponsor's proprietary measures of subject satisfaction may not be adequately validated or widely available
- The definition of clinically meaningful outcome increasingly depends on patient preferences and expectations as new indications for use emerge.

Patient Preference Information (PPI)

- PPI is useful in evaluating a device's benefit-risk profile when patient decisions are considered to be "preference sensitive"
- As an example, for a facial contouring indication, each patient has specific aesthetic goals and a certain tolerance level for risk.

Questions to Panel

FDA proposes that study sponsors use publicly available validated clinician-reported outcomes (ClinROs) and patient-reported outcomes (PROs) to improve clinician-reported and patient-reported effectiveness outcomes across dermal filler studies, which may be accomplished by:

- Study sponsors publishing the ClinRO and PRO used in their clinical study
- Study sponsors submitting their ClinRO and PRO to the MDDT program

The Panel will be asked for recommendations on the development of publicly available outcomes measures for dermal filler studies, and how to facilitate comparisons of effectiveness outcomes across dermal fillers.

Patient Perspective

- While PRO measures provide patient's own assessment of an outcome at a given point in time, they do not convey patient values.
- Dermal fillers are used in elective procedures for which the patient is the end user
- Patient perspective on benefit and tolerance for risk should be incorporated into effectiveness evaluations
- Clinical success may vary depending on patient demographics and the perspectives of different patient populations.

Patient Perspective

- For example, for a facial contouring indication, each patient has specific aesthetic goals and a certain tolerance level for risk of intravascular injection to achieve these goals.
- Level of acceptable risk may differ by the patient demographic, such as age, ethnicity or gender identity.
- Differing indications for treatment are also tied to patient perspective: correction of age-related changes in the lips may have different clinical success criteria compared to a patient seeking lip augmentation.

Patient Demographics

- The safety and effectiveness outcomes of a clinical study may also vary based on patient demographics.
- Current dermal filler clinical studies define the age of the intended study population, the gender distribution, and the distribution by Fitzpatrick Skin Type (FST).
- Enrolling diversity of skin types in the study helps ensure the study population is reflective of the demographics of the United States
- In recent years, the Agency has encouraged studies to include enrollment goals by FST, with at least 20% of subjects from FST IV – VI and 10% from FST V – VI.

Patient Demographics

- These enrollment goals may not be reflective of the distribution of FSTs within the U.S. population.
- Enrollment goals that better align with the demographics of the broader patient population may be appropriate for other key subgroups such as age, gender, or ethnicity.
- There may be indications where the demographics of the patient populations who are seeking specific treatments differ from that of the general US population, as well as indications where the patient demographics evolve over time (e.g. increasing representation of men).

Questions to Panel

FDA has identified the importance of the following measures to overcome the challenges associated with emerging indications for use and to encourage the incorporation of patient satisfaction and perspective into the study of dermal fillers and the informed decision-making process:

- Incorporation of patient perspective and diverse subject populations in the development of validated ClinROs and PROs
- Inclusion of enrollment goals to ensure that the study population is appropriate for the indication

The Panel will be asked to discuss factors to be considered in determining the appropriate patient populations and development of ClinROs, PROs, and clinical studies.

Questions for Panel (cont)

Prior dermal filler approvals may have been based on ClinROs and PROs that did not incorporate patient perspectives and diverse subject populations, or they may have been based on studies that enrolled only small numbers of important demographic groups such as men and those with higher FST.

The Panel will be asked to discuss incorporating patient perspectives in device labeling.

Question to Panel (cont.)

FDA proposes the proactive incorporation of patient preference information into the design of clinical studies and the approval process. This may include the incorporation of study endpoints to query subjects regarding the level of risk that is acceptable to achieve various levels of perceived benefit.

The Panel will be asked to comment on the utility of PPI in informing the benefit-risk assessment of dermal fillers.


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