Targeted Protein Degrader Safety Committee

Our Mission

To advance efficient and effective translational safety assessment to maximize the therapeutic potential of targeted protein degraders for patients by an international network of multi-partite, multi-stakeholder experts.

Chairs

Public Chairs

Dr. Lyn Jones (Dana-Farber Cancer Institute)

Private Chairs

Ruth Roberts (ApconiX), Mira Pavkovic (Bayer AG)

HESI Staff

Lucilia Mouries, Connie Mitchell

Webpage

https://hesiglobal.org/targeted-protein-degrader-safety/

2021 Committee Highlights

Geographic Representation
United State, United Kingdom, Germany, Switzerland, Denmark, France

Scientific Meetings and Trainings

1 meeting

- Despite growth in PROTAC and molecular glue therapeutic development programs, there has been limited public discussion or scientific consensus on the application of rigorous, consistent, and effective methods for assessment of their clinical safety. As a result, the progress of these programs and their ability to support critical patient populations safely and efficiently has opportunity to be enhanced. In this workshop, multiple stakeholders shared unpublished case studies to discuss challenges related to PROTACs and molecular degraders. This workshop launched our committee to try and address these challenges.
(Workshop, Virtual, 200 attendees)

Outreach, Communications

- **1** Oral Presentation, SOT 2023

  We had a session accepted for Society of Toxicology (SOT) 2023 Annual Meeting entitled “Targeted protein degradation therapeutics: opportunities and challenges” which will highlight work in this field from multiple committee members.

- **1** Oral Presentation, SPS 2022

  At the Safety Pharmacology Society (SPS) 2022 Annual Meeting we will present in a continuing education course in a presentation entitle “Targeted Protein Degraders: Introduction and Potential Safety Challenges”.

Working Groups

- **Cereblon-related Safety Challenges**
  This group is exploring challenges related to cereblon-mediated protein degradation and mapping current tools we have to evaluate those challenges (e.g., teratogenicity).
- **Study Design Challenges**
  This group is discussing assays and models used to evaluating safety and highlighting specific differences for heterobifunctional degraders and molecular glue degraders compared to traditional small molecules.

Areas of Focus for Next Year

- **Continued Public Sector Outreach**
- **Creation of Points-to-consider Framework for Safety Assessment**

Strategic Impact Areas

Enhanced efficiency and accuracy in safety assessment practice.
This committee is focused on advancing safety assessment to maximize the therapeutic potential of targeted protein degraders for patients.

Catalysis of new science.
Heterobifunctional degraders and molecular glues are a newer class of therapeutics that require special safety considerations compared to

Enhancement of the societal knowledge base on human biological processes of relevance for protecting human health.
While these molecules are being used as therapeutics, the underlying biology of the degradation pathways are sometimes unknown. This committee is also exploring what is known about specific endogenous processes, such as the role of cereblon.

Publications

Published

Targeted protein degraders: a call for collective action to advance safety assessment, Jones LH, Mitchell CA, Loberg L, Pavkovic M, Rao M, Roberts R, Stamp K, Volak L, Wittwer MB, Pettit S, Nature Reviews Drug Discovery 2022 Jun;21(6):401-402. doi: 10.1038/d41573-022-00055-9.

Participating Organizations

Gov't/Regulatory
- US FDA

Private Industry
- AbbVie
- Amgen
- ApconiX
- Bayer AG
- BMS
- C4 Therapeutics
- Foghorn Therapeutics
- Janssen
- Kymera
- LEO Pharma
- Merck
- Merck KGaA
- Novartis
- Oerth Bio
- Pfizer
- Roche
- Genentech
- Sanofi
- Schrodinger
- Takeda
- UCB

Academic/Research
- Broad Institute of MIT and Harvard
- Dana-Farber Cancer Institute