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Oncology

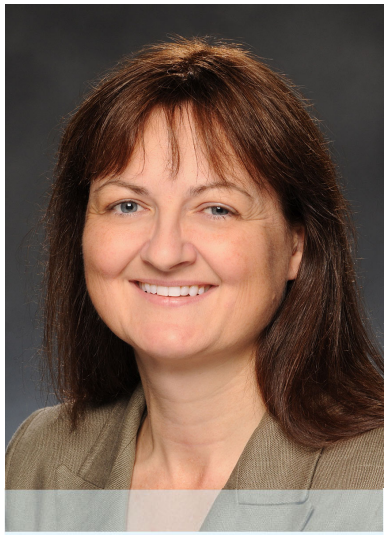
Special Interest Group

ISSUE PANEL

Clinical Evidence for Health Technology Assessment in Oncology, Are We Going Backwards?

Where Are We Going With Single-arm Trials?

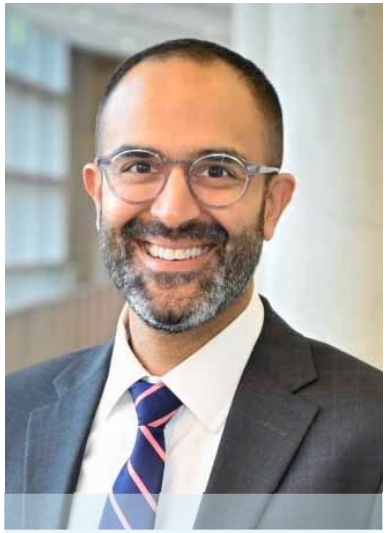
Tuesday, 8 November 2022 | 10:15-11:15



Sorrel Wolowacz, PhD

Head European Health Economics, RTI Health Solutions, Manchester, UK

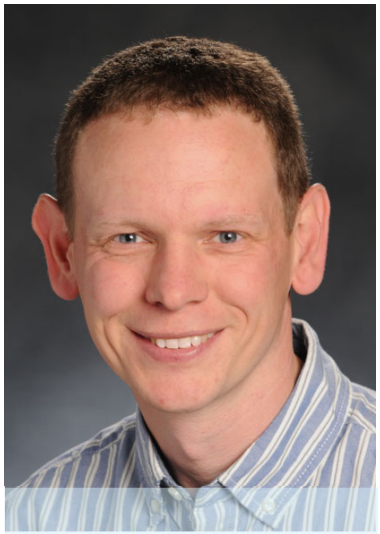
MODERATOR



Vishal Bhatnagar, MD

Associate Director for Patient Outcomes, Oncology Center of Excellence, Food and Drug Administration, Silver Spring, MD, US

PANELISTS



Adrian Vickers, PhD

Director, Data Analytics and Design Strategy, RTI Health Solutions, Manchester, UK

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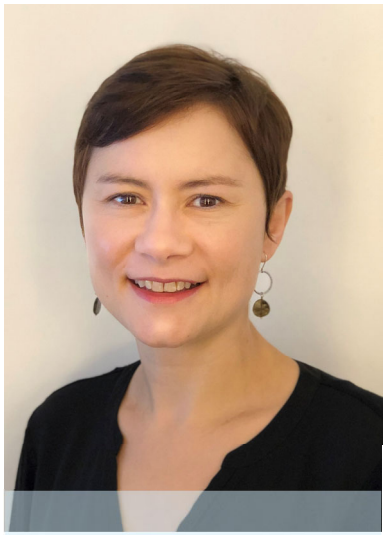


Anne-Pierre Pickaert, MSc

Specialist on HTA and patient access, Patvocates, Paris, France

PANELISTS

Many products are receiving approval based on single-arm trials

- FDA granted 153 new oncology indications based on single-arm trials between 2001 and 2020.
  - 102 accelerated and 51 regular approvals
- 32 NICE oncology appraisals between 2017 and 2022 (17%) used only single-arm trial evidence as the primary clinical evidence.
  - 91% of these (29 of 32) were recommended for use
  - Half were within the Cancer Drugs Fund

Agrawal et al. J Clin Oncol. 2021;39(15_suppl):e13572.
Zou et al. Value in Health. 2022;25(12S).

Motivations commonly cited for the use of single-arm trials

- High unmet medical need
- Avoids allocating patients to potentially less effective control therapies
- Challenges with lengthy and confounded survival endpoints
- Difficulty enrolling patients with rare tumour types
  - e.g., biomarker-defined subsets of disease

Agrawal et al. J Clin Oncol. 2021;39(15_suppl):e13572.

Single-arm trial endpoints for regulatory approval

- Response rate
  - Most common endpoint used for substantial evidence of efficacy to support approval
  - 120 of 153 FDA approvals (78%)
- Durability of response
  - Also considered as supportive evidence of clinical benefit
- Why not progression-free survival (PFS) or overall survival (OS)?
  - Tumour regression (response) can be directly attributed to the drug(s)
    - Spontaneous remission is rare to non-existent (historical control: 0%)
  - "Prolonged" stable disease, PFS, and OS in a single-arm study could be due to natural history of the tumour and not the intervention

Agrawal et al. J Clin Oncol. 2021;39(15_suppl):e13572.
Blumenthal. EMA-ESMO Workshop on single-arm trials for cancer drug market access. 2016.

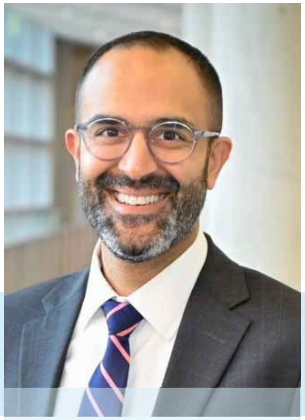
Single-arm trial data presents challenges for health technology assessment (HTA)

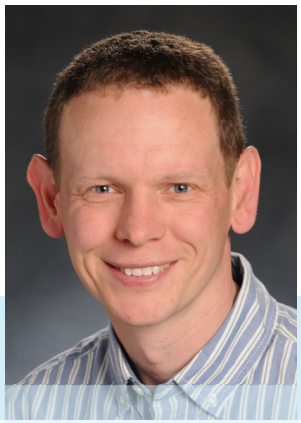
- HTA requires comparison of new interventions with current treatments.
  - Indirect comparisons are required with outcomes from other trials or real-world data
  - Differences in costs and quality-adjusted life-years must be estimated over patients' lifetimes
- Although statistical methods exist, there remains a substantial potential risk of bias.
  - Differences between studies in unknown or unmeasured prognostic factors
  - Differences between studies in the definition or ascertainment of endpoints
- Lifetime analyses require survival estimates.
  - Response endpoints may not be reliable surrogates for PFS or OS
- These issues, as well as small sample sizes, may result in substantial uncertainty in cost-effectiveness estimates.

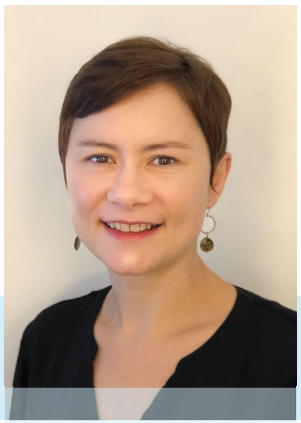
Murphy et al. Health Technol Assess. 2021 Dec;25(76):1-228.

Are we making progress towards higher quality clinical evidence for HTA in Oncology?

- Health economists and outcomes researchers have long called for evidence reflecting effectiveness in routine practice (e.g., pragmatic trials).
- Progress towards this approach has been very limited.
- Rather, with increased use of single-arm trials, are we going backwards?







1 Panel presentations

Vishal Bhatnagar, MD
FDA perspective

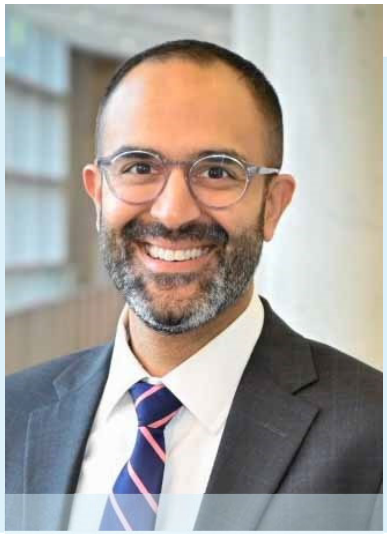
Adrian Vickers, PhD
Statistical perspective

Anne-Pierre Pickaert, MSc
A patient perspective

2 Open debate –
Panel and audience (~15 min)

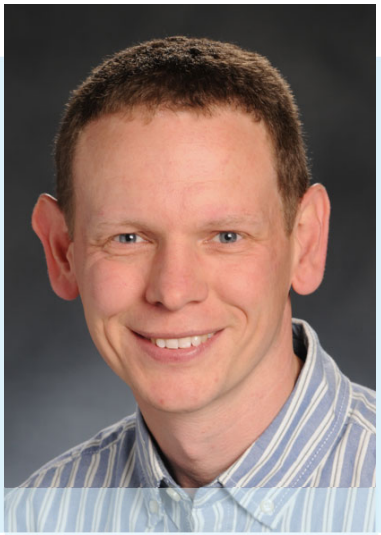
3 Audience poll –
With the increased use of single-arm trials as the primary evidence for oncology HTAs, are we going backwards?

Many thanks to our panel and to you, the audience, for your thoughts!



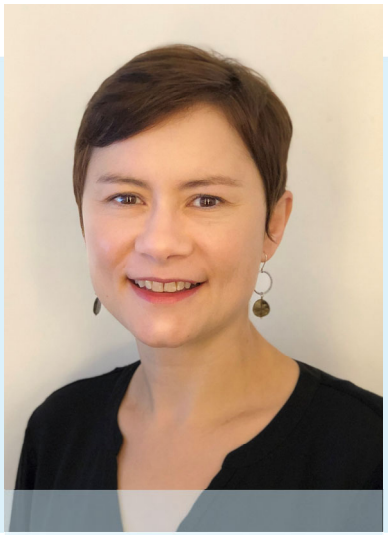
Vishal Bhatnagar, MD

FDA perspective



Adrian Vickers, PhD

Statistical perspective



Anne-Pierre Pickaert, MSc

A patient perspective

It’s time for the poll!

With the increased use of single-arm trials as the primary evidence for oncology HTAs, are we going backwards?

- Yes
- No
- Maybe
- Don’t know

ADVANCE TO NEXT SLIDE FOR THE POLL

Join us to continue the discussion…

- *Discussion group – 11:45 am today, Discussion Lounge, Exhibit Hall – X1*

Look out for other sessions…

- *Podium session 228 – 1:30 pm today,*
  "Innovative Methods in Indirect Treatment Comparisons"
- *Issue Panel 27 – 10 am tomorrow,*
  "External Control Arms, Is It the Way to Go?"