

Peer Review

Review of: "Progression-Free Survival as a Primary End-Point: Counting the Cost"

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1. Oversimplification of Surrogate Endpoint Validity

The manuscript strongly argues that PFS is often unreliable but does not sufficiently acknowledge that:

Surrogacy strength varies significantly across cancer types.

In some malignancies (e.g., hematological cancers, targeted therapy settings), PFS demonstrates strong predictive validity for OS.

Suggested Revision

Include cancer-specific stratification:

Strong surrogate contexts

Moderate surrogate contexts

Weak surrogate contexts

2. Lack of Structured Evidence Synthesis

The commentary relies primarily on selected illustrative trials rather than systematic evaluation or graded evidence analysis.

This limits scientific robustness and increases the risk of selection bias.

3. Limited Discussion of Evolving Oncology Trial Design

Modern oncology trials incorporate:

Adaptive trial designs

Composite endpoints

Real-world evidence integration

Patient-reported outcomes

These developments should be discussed to provide a balanced perspective.

4. Insufficient Consideration of Post-Progression Treatment Effects

One of the main reasons OS benefit is difficult to demonstrate is:

Multiple subsequent treatment lines

Treatment cross-over

Improved salvage therapies

These confounders justify partial reliance on PFS and require discussion.

Declarations

Potential competing interests: No potential competing interests to declare.