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Research Ethics in Medicine Study Group

JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE

Risk and benefit for basket clinical trials in oncology: a systematic review with meta-analysis

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Background

Basket clinical trials (BCTs):

- are human research studies commonly used in precision oncology.
- simultaneously test a therapeuticintervention for multiple malignancy types under the same study protocol.

Patients with different cancers recruited to BCT share specific molecular characteristics which are predictive of clinical benefit from the experimental treatment.

Little is known about the risk/benefit ratio in BCTs.

Objective

Our aim was to evaluate risks and benefits in cancer BCTs.

Methods

The study protocol was prospectively registered in PROSPERO. We systematically searched Embase, PubMed, and ClinicalTrials.gov for interventional cancer BCTs. We included targeted therapy and/or immunotherapy studies of all cancer types. We measured risk using drug-related grade 3 or higher adverse events (AEs), and benefit by objective response rate (ORR), progression-free survival, and overall survival.

Results

We identified **126** arms of **75** BCTs (7,659 patients) that met our eligibility criteria (Fig. 1). The overall fatal treatment-related AE rate (grade 5) was **0.7%**, and **30.4%** of patients experienced grade 3-4 drug-related toxicity. The overall drug-related grades 3-5 AE rate was higher for targeted therapies than immunotherapies: **31.7%** vs **7.9%**, p=0.004 (Table 1). The pooled overall ORR was **18.0%** and was lower in solid tumours, **17.5%**, compared with haematological malignancies, **63.6%**; p = 0.004. The ORR for targeted therapy agents was **17.9%**, and for immunotherapy agents, ORR was **19.1%**. The median progression-free survival was **3.1 months**, and the median overall survival was **8.9 months**.

Conclusions

Cancer patients should be properly informed about the benefits and risks in BCTs. While we acknowledge that our systematic analyses do not cover all aspects related to benefits and risks in cancer BCTs, we note that efforts should be made to improve the data reporting that allows for such assessments.

In basket clinical trials nearly **four out of five** participants did not respond to treatment, **one in 135** died because of drug toxicity, and nearly **one third** experienced grade 3 or grade 4 drug-related adverse events.

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Fig. 1 Flow diagram with number of identified, screened and included records.

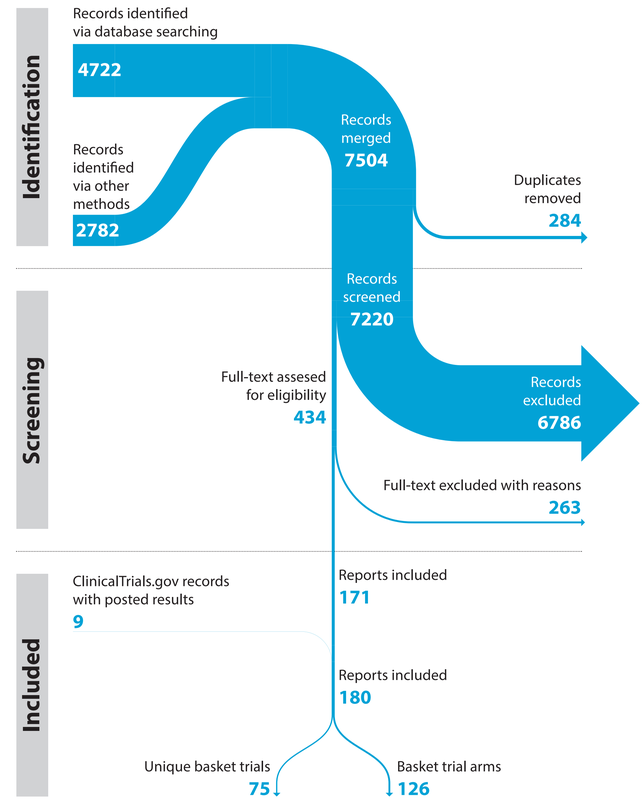

Table 1 Pooled estimates of risk and selected benefit measures in targeted therapy and immunotherapy studies.

	Type of therapy	
Pooled estimate	Targeted therapy	Immunotherapy
Objective response rate	**17.9%**	**19.1%**
Drug-related Grades 3-4 AEs rate	**32.9%**	**7.6%**
Drug-related Grades 3-5 AEs rate	**31.7%**	**7.9%**
Drug-related Grades 5 AEs rate	**0.7%**	**1.2%**

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Conflict of Interest

Simon Van Wambeke receives funding from IPSEN (travel and accommodation) and Janssen-Cilag (travel and accommodation; fees). Other authors declare no conflicts of interest.

Funding

This project is funded by National Science Center, Poland, UMO-2019/35/N/HS1/00178, UMO-2021/41/B/HS1/01123 (www.ncn.gov.pl)

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