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Original Research

A pooled analysis of published, basket trials in cancer medicine

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Abstract ***Background:*** There is widespread interest in cancer basket trials. However, to date, there has been no formal analysis of all published basket trials.
Methods: We performed a systematic review to identify all published basket trials in cancer medicine. We included studies that (1) did not place restriction on tumour type and (2) used a biomarker for the basis of enrolment (3) administered at least one anti-cancer agent in prospective fashion and (4) reported responses by each tumour type included. We sought information regarding the tumour histology included and the response rate in basket trials. In addition, we used national cancer statistics to identify which tumour types have been overrepresented in basket studies (i.e. more representation in trials than their incidence would suggest) and those which are under-represented.
Results: We identified eight articles with a combined enrolment of 1176 patients were included in our analysis, representing over 33 tumour types. Ovarian and fallopian tube cancers 221/1176 (19%), colorectal cancer 144/1176 (12%) and sarcoma 129 (11%) were the most common tumours represented, whereas renal cell cancer, seminoma, thymic carcinoma and neuroendocrine tumour and appendiceal carcinoma were the least represented with one case each. The overall response rate was 25%. Common cancers may be underrepresented compared with rarer tumour types (linear regression beta = 0.58, 95% confidence interval = −0.037–1.21) (slope < 1 implies under-representation, >1 over-representation).
Conclusions: We found that, to date, over 1100 patients have been enrolled on published basket studies. Common cancers may be underrepresented compared with rarer tumours. The

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overall response rate was 25%. Patients enrolling on basket trials should be counselled appropriately that although these studies are highly promising, most patients did not respond. Future targets and drugs may improve on these results.

1. Introduction

There is widespread interest in cancer basket trials [1–4], which are thought to accelerate the promise of precision medicine [5]. Basket trials are defined as those which include cancer patients, with diverse tumour tissues of origin, who share a molecular aberration or biomarker [1] and are treated with a single therapy. As example, in a seminal basket trial, Hyman et al [6] administered vemurafenib, a BRAF-inhibitor, to cancer patients with BRAF V600 mutations of diverse histology. The authors found several tumour types in which vemurafenib was effective (Erdheim–Chester disease or Langerhans'-cell histiocytosis and non-small-cell lung cancer (NSCLC)), and some where it was not (multiple myeloma, pancreatic cancer). More recently, an inhibitor of tropomyosin receptor kinase fusions was tested in diverse tumours, with impressive results [7].

While there have been numerous review articles and commentaries regarding basket studies, to date, there has been no formal analysis of all published basket trials. For this reason, we set out to perform a systematic overview of published basket trials. Specifically, we sought information regarding the tumour histology included, and the response rate in basket trials. We used national cancer statistics to identify which tumour types have been overrepresented in basket studies (i.e. more representation in trials than their incidence would suggest), and those which are under-represented.

2. Methods

2.1. Overview

We sought to assemble a collection of basket trials that (1) did not place restriction on tumour type and (2) used a biomarker eligibility criterion for the basis of enrolment (3) administered at least one anti-cancer agent in prospective fashion and (4) reported responses by each tumour type included.

2.2. Literature search

We searched Google scholar for the terms cancer and basket trial on 31st March 2018. We searched MEDLINE for basket and neoplasm or neoplasms or oncology on 30th March 2018 date to identify relevant basket studies. We excluded ongoing basket trials, which did not present results or review articles or articles that discuss basket trials in general. We included basket studies if they met the four aforementioned criteria. A consort diagram is available in the Supplemental Appendix.

Table 1
Characteristics of patients included in published cancer basket studies to date.

Characteristic	Number of patients (%)
Median age (range) (yrs)	56 (0.3–86)
Total Patients	1176
Sex no. (%)	
Male	421 (36)
Female	755 (64)
Biomarker/mutation present (%)	
AKT	58 (5)
HER2	276 (24)
HER3	16 (1)
TPK	55 (5)
MMRD	86 (7)
BRAF	171 (15)
Hedgehog	21 (2)
EGFR	9 (1)
BRCA	298 (25)
KIT, PDGFRA, PDGFRB	186 (16)
Therapy given (%)	
Imatinib	186 (16)
AZD5363	58 (5)
Neratinib	141 (12)
Olaparib	298 (25)
Vemurafenib + Cetuximab	27 (2)
Pembrolizumab	86 (7)
Larotrectinib	55 (5)
Trastuzumab plus pertuzumab	151 (13)
Vemurafenib	144 (12)
Erlotinib	9 (1)
Vismodegib	21 (2)
Patients with response to therapy-no. (%)	290 (25)
Response rate per study (%)	**RR (%)**
Phase II, open-label study evaluating the activity of imatinib in treating life-threatening malignancies known to be associated with imatinib sensitive tyrosine kinases	13.0
AKT inhibition in solid tumours with AKT1 mutations	24.0
HER kinase inhibition in patients with HER2- and HER3-mutant cancers	11.0
Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation	26.0
Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations	15.0
Mismatch-repair deficiency predicts response of solid tumours to PD-1 blockade	54.0
Efficacy of larotrectinib in TRK fusion– positive cancers in adults and children	80.0
Targeted therapy for advanced solid tumours on the basis of molecular profiles: results from MyPathway, an open-label, Phase IIa multiple basket study	22.0