Addressing Key Challenges in the Setting of Tumor-Agnostic Drugs:

Meeting an Unmet Need?

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ISPOR 2024 Atlanta
Workshop 310
Wednesday, May 8, 2024

THE CHOICE INSTITUTE
School of Pharmacy

Disclosures

No conflicts of interest related to this presentation

Promise of a New Era!

FDA grants accelerated approval to pembrolizumab for first tissue/site agnostic indication

May 30, 2017

- Microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumors
- Histology-independent therapies[1]
- Potential advantages: lower trial costs, earlier patient access
- Panel gene testing or NGS identifies patients likely to benefit.[2]

[1] PMID: 38176220. [2] PMID: 33745759;
NGS: Next generation sequencing

It´s Time for Our First Poll!

How many tissue-agnostic therapies has the FDA approved to date?

a) 1-2
b) 3-5
c) 6-9
d) ≥ 10

It´s Time for Our First Poll! - Answer

How many tissue-agnostic therapies has the FDA approved to date?

a) 1-2

b) 3-5

c) 6-9 ← **7**[1]

d) ≥ 10

EMA: 2 approvals[2]

NICE: 20+ in pipeline (2020)[3]

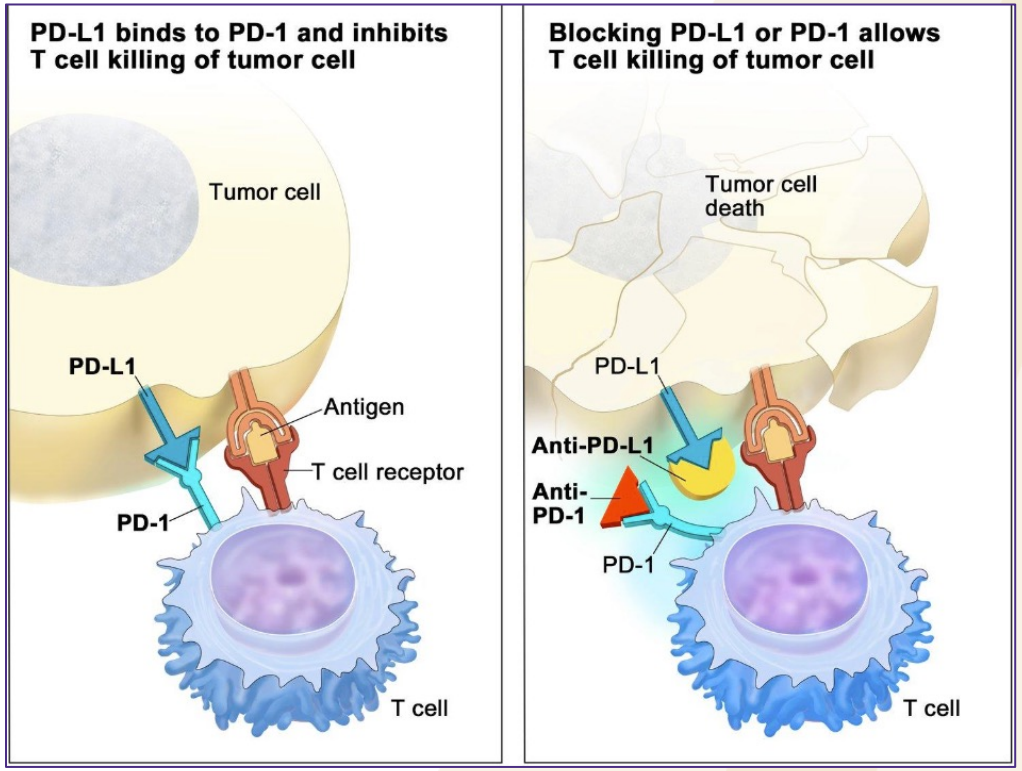
[1]FDA:https://www.sabcsmeetingnews.org/tumor-agnostic-therapies-advance-possibilities-for-precision-medicine/.

[2]EMA: https://www.pharmaceutical-technology.com/news/ema-bayers-ntrk-vitrakvi/ .

[3]NICE: Accelerated Access Collaborative. NGS = Next generation sequencing

New Era Fraught with Challenges - Biology

- Incomplete understanding of functional/ pathological significance of biomarkers; not always prognostic drivers of disease.
- Histologies differ in natural histories, treatment patterns, drug response.
- Despite heterogeneity, equitable access at top of our minds.
- Hazards of rapid drug approval are not new...

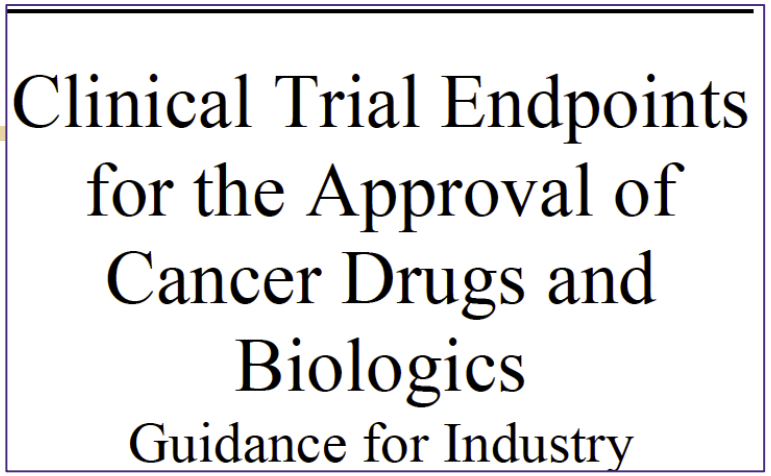


New Era Fraught with Challenges - Methods

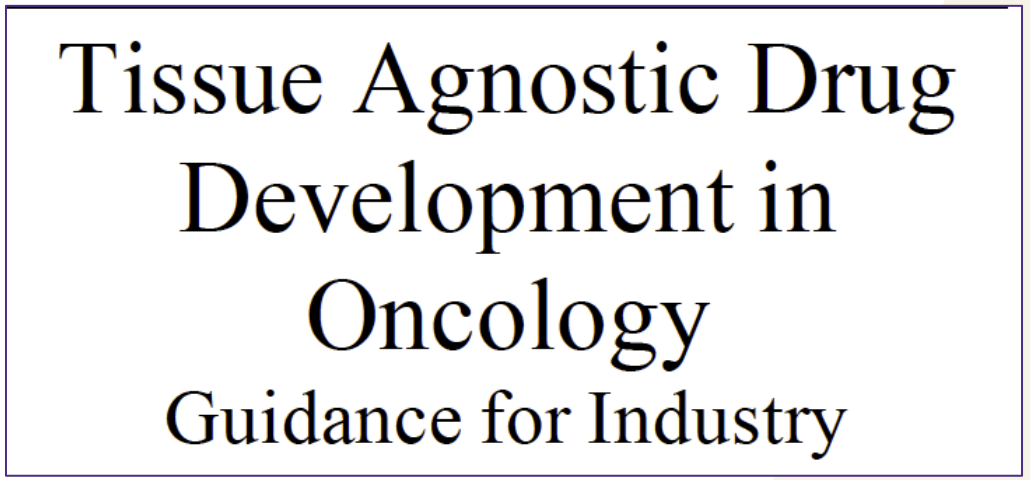
- Rare cancers (small sample sizes)
- Infeasible to conduct randomized clinical trials
- No comparison (control) group
- ´Basket trials´
- Heterogeneity – histologies, patient baseline risk, costs
- Intermediate outcomes, may not predict survival

- Need for novel therapeutic agents is great
- Must provide robust clinical evidence

FDA Center of Excellence Guidance Documents



December 2018



October 2022

March 2022

March 2023

Guidance from the United Kingdom

CANCER

- **optimised** – the medicine is only available for certain people with a condition
- **recommended for use within the cancer drugs fund (CDF)** - the medicine can become available via the CDF so that we can be sure it is effective
- **only in research** – you can only have the medicine as part of a clinical trial, so researchers can collect more evidence about how well it works
- **not recommended** - the medicine should not be available

Final Research Report

Modelling approaches for histology-independent cancer drugs to inform NICE appraisals

Modelling approaches for histology-independent cancer drugs to inform NICE appraisals

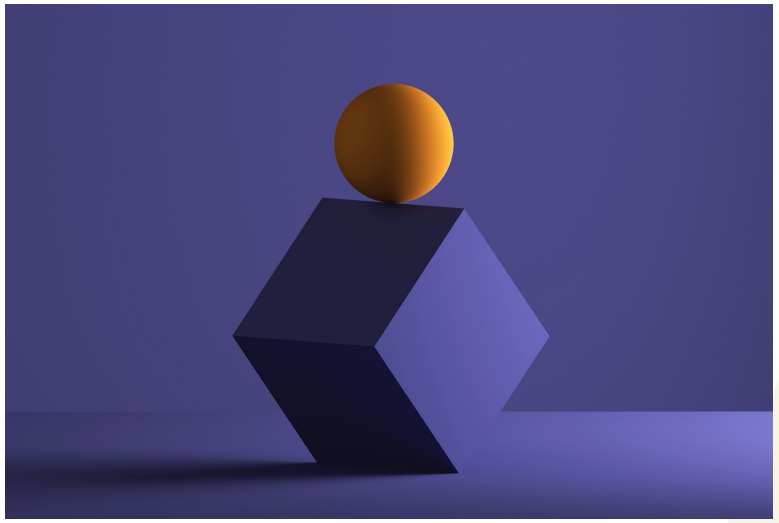
Produced by	CRD and CHE Technology Assessment Group, University of York, Heslington, York YO10 5DD ScHARR Technology Assessment Group, University of Sheffield, Sheffield, S1 4DA

[1]https://www.cancerresearchuk.org/about-cancer/treatment/access-to-treatment/cancer-drugs-fund-cdf.
[2]https://www.cancerresearchuk.org/funding-for-researchers/our-research-infrastructure/our-centre-for-drug-development/determine-overview. [3]Murphy, et al.

Guidance from the European Union

[1]https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/accelerating-clinical-trials-eu-act-eu
[2]https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview.
[3]https://health.ec.europa.eu/non-communicable-diseases/cancer/europes-beating-cancer-plan-eu4health-financed-projects/projects/pcm4eu_en#:~:text=PCM4EU%20%2D%20Personalised%20Cancer%20Medicine%20for%20all%20EU%20citizens&text=As%20PCM%20is%20based%20on,implementation%20of%20the%20PCM%20approach.

Workshop Focus



- Leverage established and novel biostatistical and economic modeling methods...
- to assess novel therapies...
- to inform reimbursement decisions

ISPOR Initiatives

#1 RWE
#4 Fostering innovation
#6 Accelerated drug approvals
#9 Precision medicine

...plus
upcoming Task Force Report on Surrogate Biomarkers