WECAN SmartStart in Cancer Patient Advocacy

WECAN MASTERCLASS in Cancer Patient Advocacy

The clinical trials we want!

- How to find, select and shape trials that are actually good for your patients.
- Beware fake news- false beliefs others want you to fall for and essential information they omit.

Bettina Ryll MPNE

Overview of the session

- Why clinical trial matters
- How to find clinical trials
- How to select clinical trials
- How to shape clinical trials

Expectation management wrt clinical trials

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Patient advocates are traditionally expected to

- fundraise for clinical research
- advertise for clinical trials
- recruit for clinical trials
- not to challenge the system
- focus on traditional topics

- be grateful

Patient voice

FEET

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Pet Hate # 200 - Moral High Horses

I think drugs are terrible.

Man, I'm just a high horse - not a morally high one.

A patient perspective

- How to use clinical trials to improve your chances to survive
- How to make sure that patients only have good trials to choose from

Patients are an own stakeholder group with overlapping and non-overlapping interests with any other stakeholder group.

Science matters

- There will always be patients with advanced cancer.
- Medical progress depends on scientific progress.

but

- Not all Science is good.
- And not every human price is justifiable.

Just because it's called 'Science' doesn't mean it's good let alone ethical.

Known officially as the Tuskegee Study of Untreated Syphilis in the Negro Male, the study began at a time when there was no known treatment for the disease.

https://www.history.com/news/the-infamous-40-year-tuskegee-study

Know your rights- the Helsinki Declaration

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Patient interest FIRST.

7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

9. It is the duty of physicians who are involved in medical research to protect the life, health,

Free to join, free to leave.

26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

Know your traditions- why you should care about a guy who lost his head.

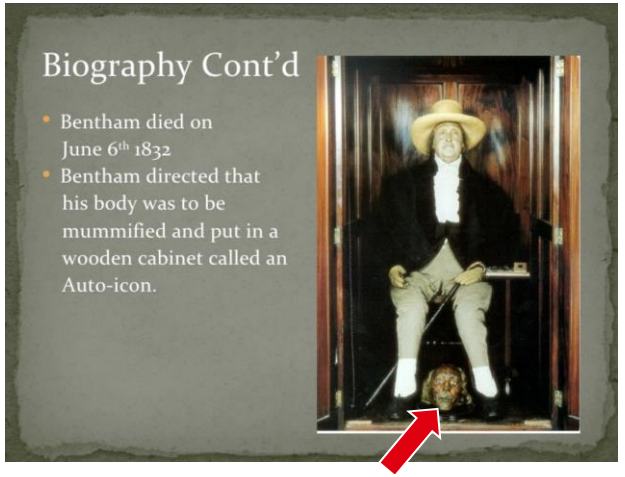
Individual versus utalitarian traditions- 'is it ok to sacrifice the individual for the 'greater good' of society?'

≠ Helsinki declaration: clearly individualistic perspective.

People will argue what is convenient for them.

Know where you stand.

A solution has to take BOTH the individual as well as the societal perspective into account.



https://www.slideshare.net/alannamlawson/jeremy-bentham-13121787

How to find clinical trials- important to know

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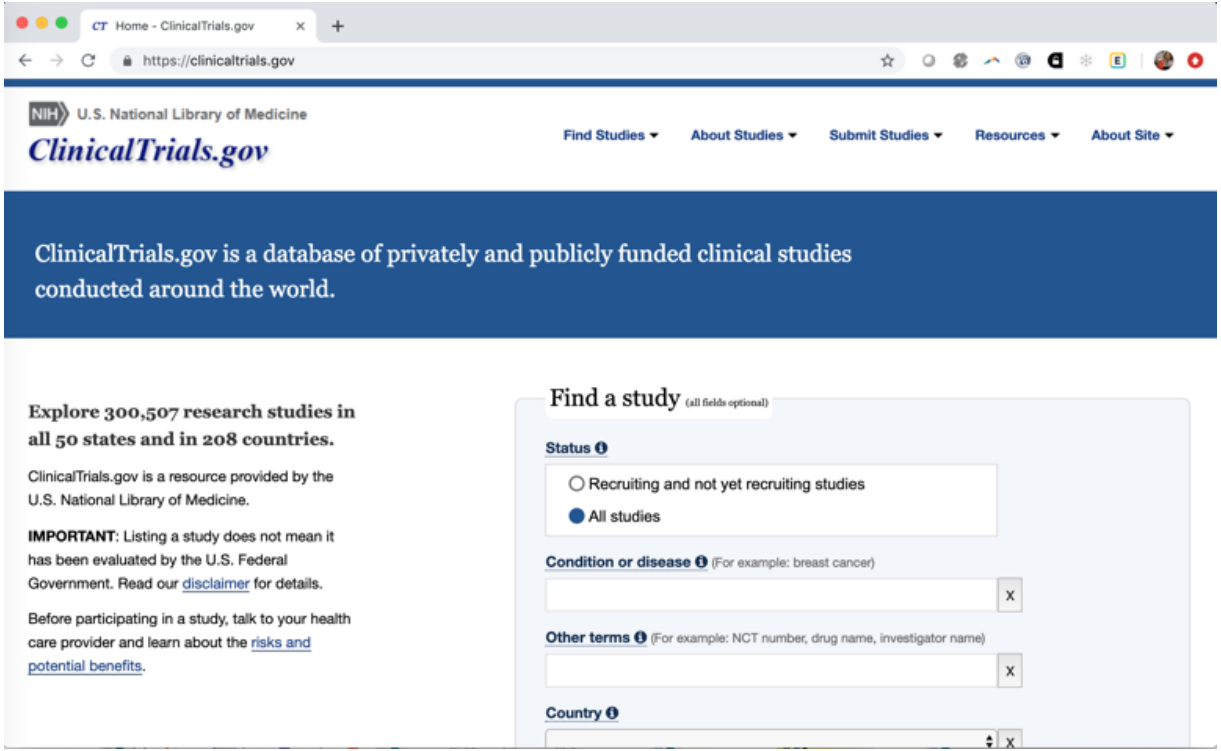
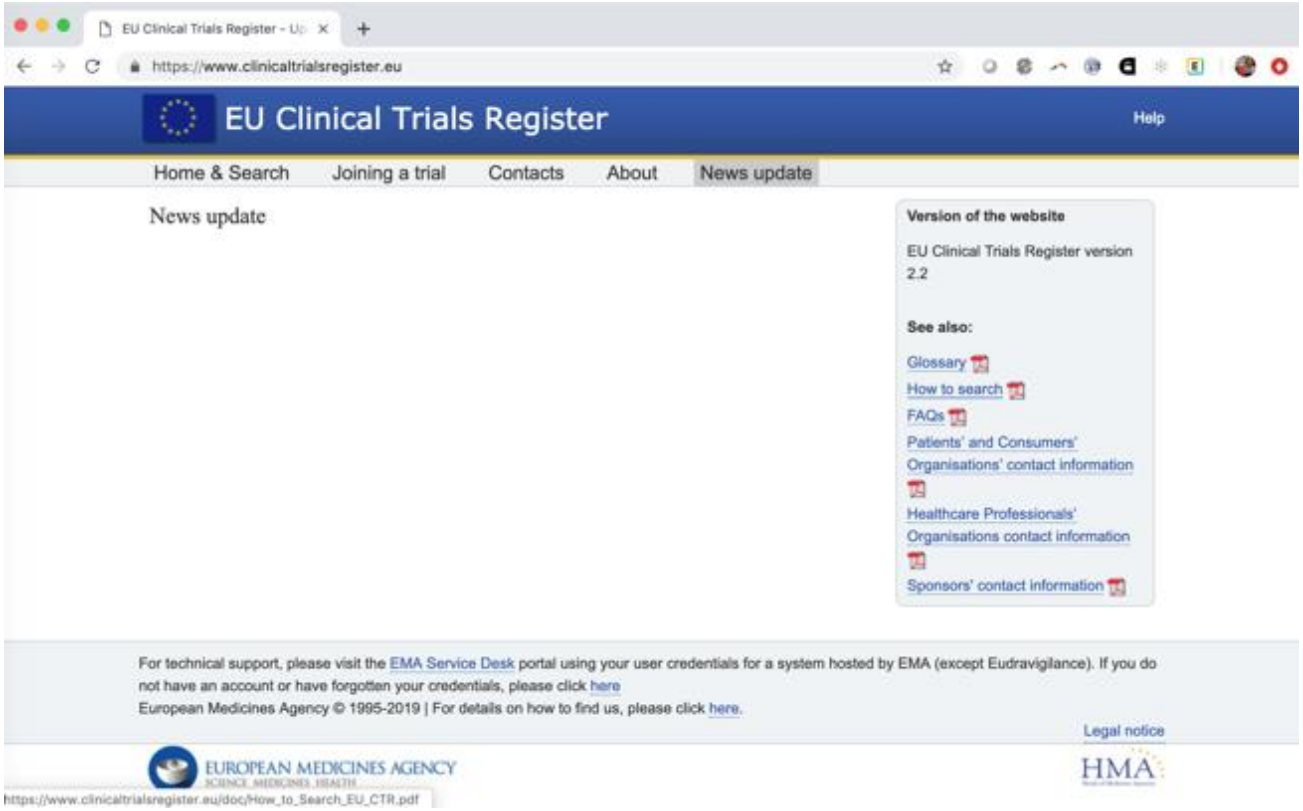
- Clinical trials need to be registered - find that database
- Avoid biased databases- e.g. maintained by single sponsors
- Beware financial motivations for matching patients to trials
- Be aware of filters and biased search algorithms- e.g. geographical, indications (‘Melanoma’ vs ‘solid tumour’)

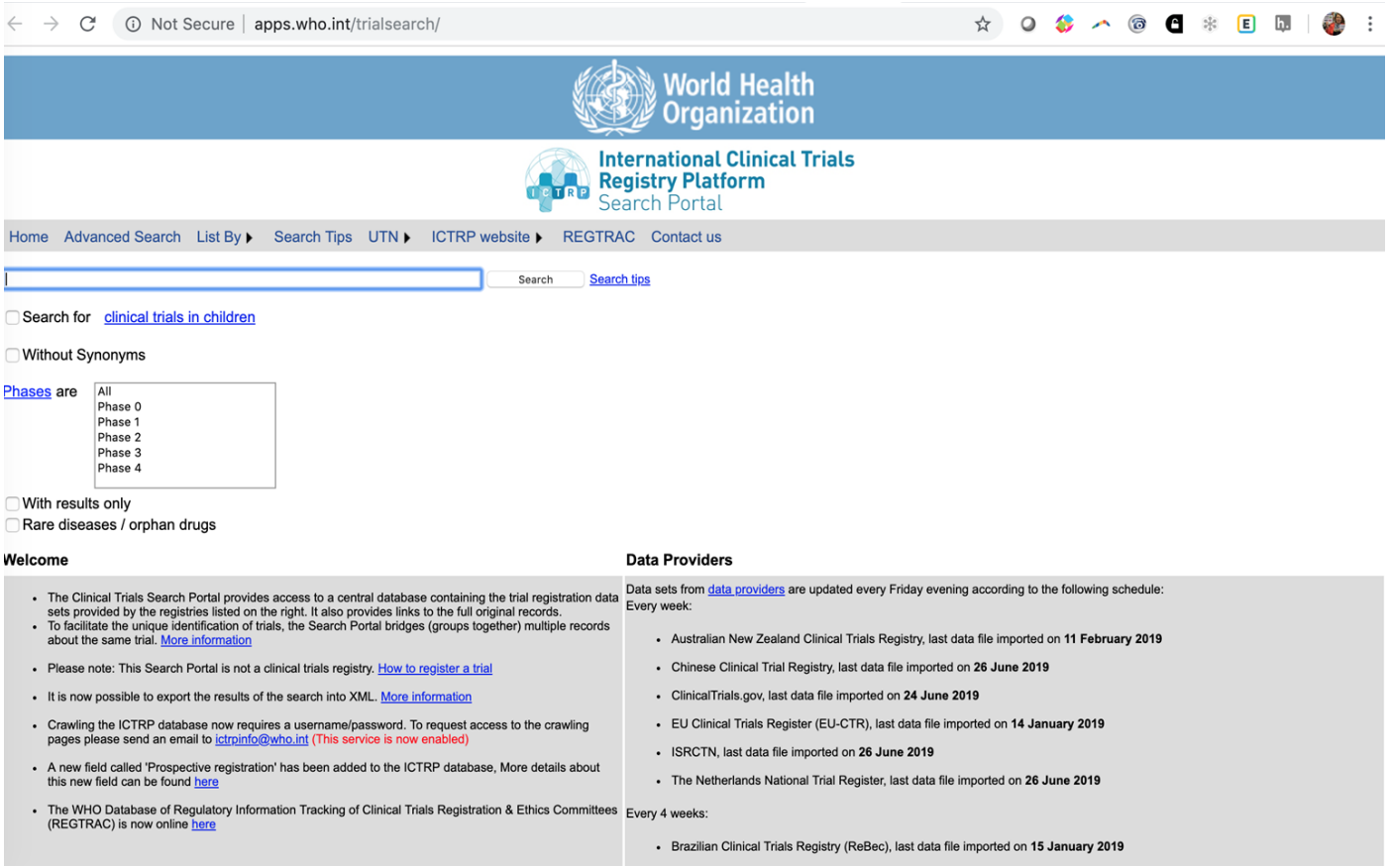
US- Clinicaltrials.gov



Europe- EUCTR



WHO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World Health Organization
International Clinical Trials Registry Platform
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Search for clinical trials in children
Without Synonyms
Phases are
All
Phase 0
Phase 1
Phase 2
Phase 3
Phase 4
With results only
Rare diseases / orphan drugs
Welcome
The Clinical Trials Search Portal provides access to a central database containing the trial registration data sets provided by the registries listed on the right. It also provides links to the full original records.
To facilitate the unique identification of trials, the Search Portal bridges (groups together) multiple records about the same trial. More information
Please note: This Search Portal is not a clinical trials registry. How to register a trial
It is now possible to export the results of the search into XML. More information
Crawling the ICTRP database now requires a username/password. To request access to the crawling pages please send an email to ictrpinfo@who.int (This service is now enabled)
A new field called 'Prospective registration' has been added to the ICTRP database, More details about this new field can be found here
The WHO Database of Regulatory Information Tracking of Clinical Trials Registration & Ethics Committees (REGTRAC) is now online here
Data Providers
Data sets from data providers are updated every Friday evening according to the following schedule:
Every week:
Australian New Zealand Clinical Trials Registry, last data file imported on 11 February 2019
Chinese Clinical Trial Registry, last data file imported on 26 June 2019
ClinicalTrials.gov, last data file imported on 24 June 2019
EU Clinical Trials Register (EU-CTR), last data file imported on 14 January 2019
ISRCTN, last data file imported on 26 June 2019
The Netherlands National Trial Register, last data file imported on 26 June 2019
Every 4 weeks:
Brazilian Clinical Trials Registry (ReBec), last data file imported on 15 January 2019

ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site

Home > Search Results > Study Record Detail

Save this study

Trial record **5 of 27** for: bms | Recruiting Studies | Melanoma

« Previous Study | Return to List | Next Study »

A Study of NKTR-214 Combined With Nivolumab vs Nivolumab Alone in Participants With Previously Untreated Inoperable or Metastatic Melanoma

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03635983

Recruitment Status : Recruiting
First Posted : August 17, 2018
Last Update Posted : June 19, 2019

See Contacts and Locations

Sponsor:
Bristol-Myers Squibb

Collaborator:
Nektar Therapeutics

Information provided by (Responsible Party):
Bristol-Myers Squibb

Arms and Interventions

Go to

Arm	Intervention/treatment
Experimental: Combination NKTR-214 + Nivolumab	Biological: NKTR-214 Specified dose on specified days Other Names: • Bempegaldesleukin • **BMS**-986321 Biological: Nivolumab Specified dose on specified days Other Names: • Opdivo • **BMS**-936558
Experimental: Monotherapy Nivolumab	Biological: Nivolumab Specified dose on specified days Other Names:

BUT
beware incomplete, inconsistent or fraudulent information

'The difference between medicine and poison is the dose'

How to select clinical trials- important to know

- **Understand your motivation**
- **Understand the underlying Science**

How to select clinical trials- what's the motivation?

- **Is it a clinical trial you are looking for?**

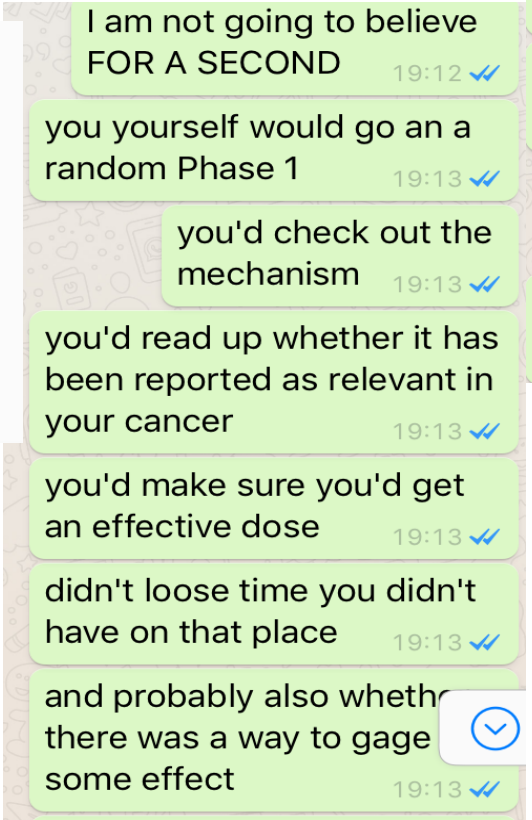
- **Why are you looking for a clinical trial?**
- Standard of care insufficient
- All lines of therapy exhausted
- Drugs not reimbursed
- ?

- **Treatment option**
- **Access**

Why patients join clinical trials

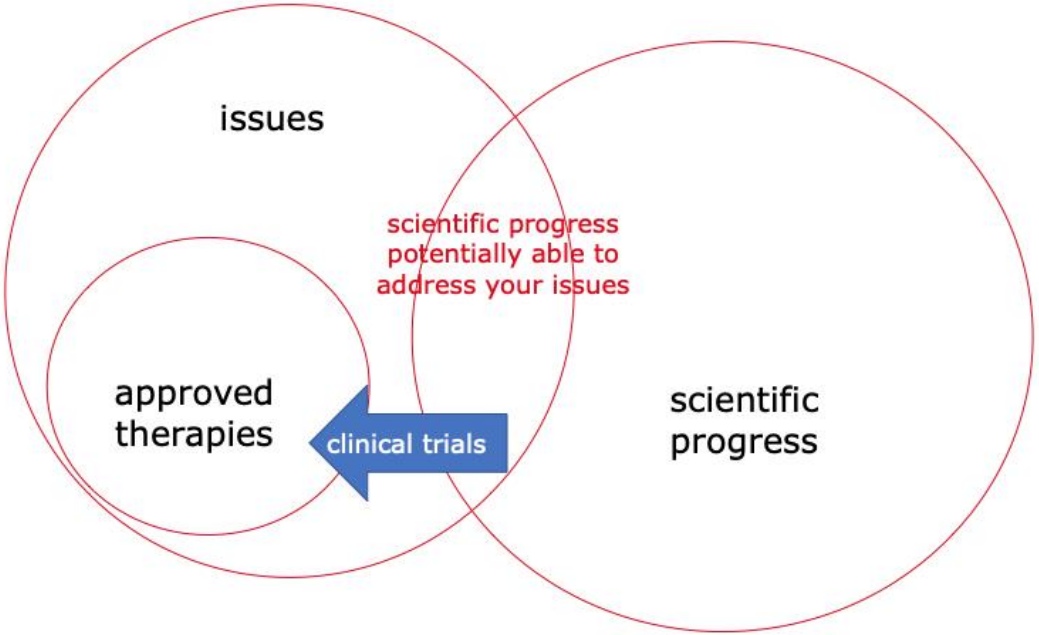
Than again, I believe that you should never enter a phase I trial and expect a benefit but with the aim to help (hopefully) future patient who might have a benefit in future trials or from approved treatment.

different rules for different people



Well I have met patients who at least claim they are altruistic and want to ad to science.
The rest I agree on. You should always get as much info as possible regarding possible effects etc. 19:17

Know your treatment and scientific landscape

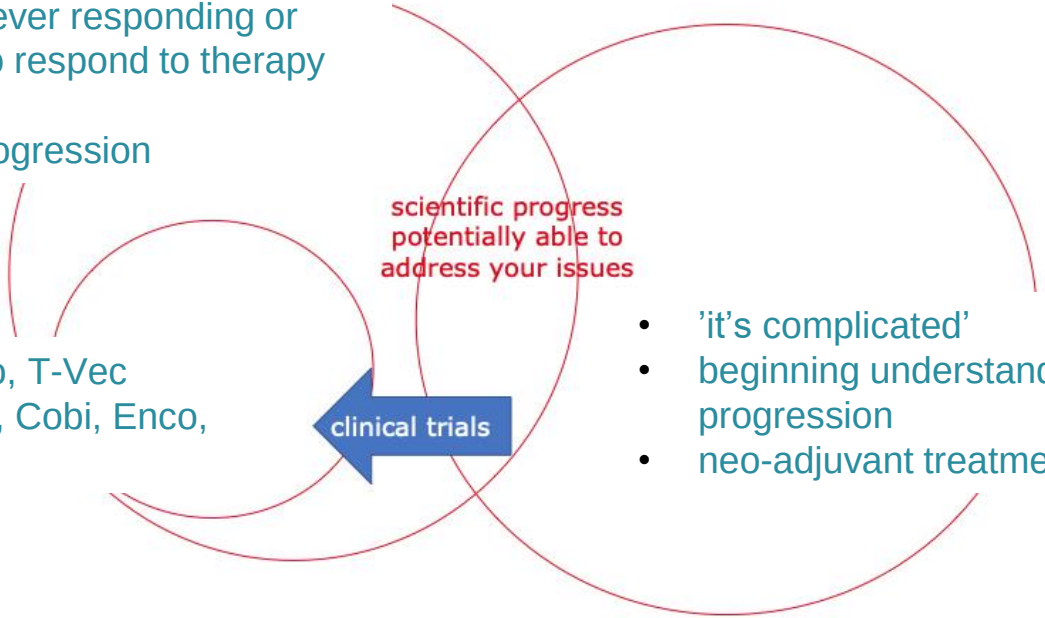


Follow Scientific news

- Pubmed- biomedical publications
- Google scholar
- Subscription services: https://ecancer.org/, ASCO, ESMO, NEJM, Lancet
- Google alerts, Google scholar alerts
- Medical journals directly- always something one misses
- Attend scientific meetings

Know your treatment and scientific landscape

- Patients never responding or stopping to respond to therapy
- brain mets
- prevent progression



- Ipi, Pembro, Nivo, T-Vec
- Dab, Tram, Vem, Cobi, Enco, Bini

- 'it's complicated'
- beginning understanding of risk for progression
- neo-adjuvant treatment

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How to choose a clinical trial

Clinical trial elements to watch out for

- what do you know about the drug?
- randomisation
- placebo
- blinding
- cross-over

Uneven randomisation, blinding, early interim analyses, cross-over, in particular when uni-directional: expect one arm to perform considerably better than the other.

CTC- How to choose when you are the patient

- Choose a design where you get the drug you want: EAP? Phase 2 after a good Phase 1?
- Avoid placebo/ nocibo because you cannot recover time lost in useless therapies
- If that’s not possible, find at least a trial with cross-over

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Shaping clinical trial design

Why care about clinical trial design?

- Earliest access to new medicines
- New doesn’t mean better- mind your risk mitigation strategy
- Trials are designed to answer population-based questions. We are individuals.
- Rules and methods evolve constantly- they are NOT set in stone.

Understand the clinical trial ecosystem- everyone has vested interests

- Pharmaceutical Industry- financial
- Regulators – SAFETY, efficacy
- HTA and payors- financial, social justice
- Clinicians and hospitals- financial, publications, careers
- NYDs (not-yet-diagnoseds)- financial, sense of security

'There is no group of angels'
Anna Wagstaff, WECAN 2019

Pet Hate # 200 - Moral High Horses

I think drugs are terrible.

Man, I'm just a high horse - not a morally high one.

My personal baseline assumptions- (only) slightly exaggerated.

- Clinicians don't understand statistics, unconventional data sources nor HTA.
- Statisticians don't understand oncology.
- Pharma is risk-averse, it's always the regulator's fault, but you can count on financial motives.
- HTAs don't understand Molecular Biology.
- Payers are the real shadow emminence.
- Everyone has vested interests.
- Everyone blames the person that is NOT in the room.
- **There are outliers in every place.**
- No one has money. Academics have less money than Pharma.
- No one has time. Pharma has less time than Academics.
- People design trials for OTHERS, not for themselves.
- **Patients are upsetting the current system.**
- **Patients aren't here to die on clinical trials.**
- **Clinical trials that don't recruit get amended.**

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Do we need more clinical trials?

Numbers of trials using common combo strategies:

1. Anti-CTLA-4 agents: 251
2. Chemotherapies: 170
3. Radiotherapies: 64
4. Anti-VEGFA agents: 43
5. Chemoradiotherapy combos: 42

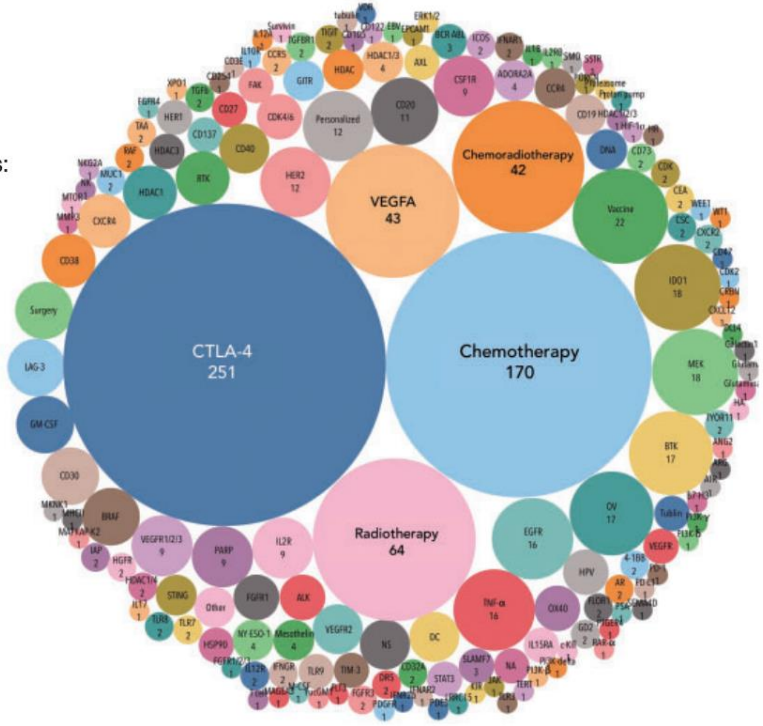

Figure 7. The landscape analysis of targets of anti-PD-1/L1 combination trials. The size of the bubble correlates to the number of trials.

https://www.ncbi.nlm.nih.gov/pubmed/29228097

2018

So unless you already got a side-effect free cure for your cancer, research always answers what your patients need and want and your patients are queuing to join clinical trials...

> The definition of insanity is doing the same thing over and over again and expecting a different result.

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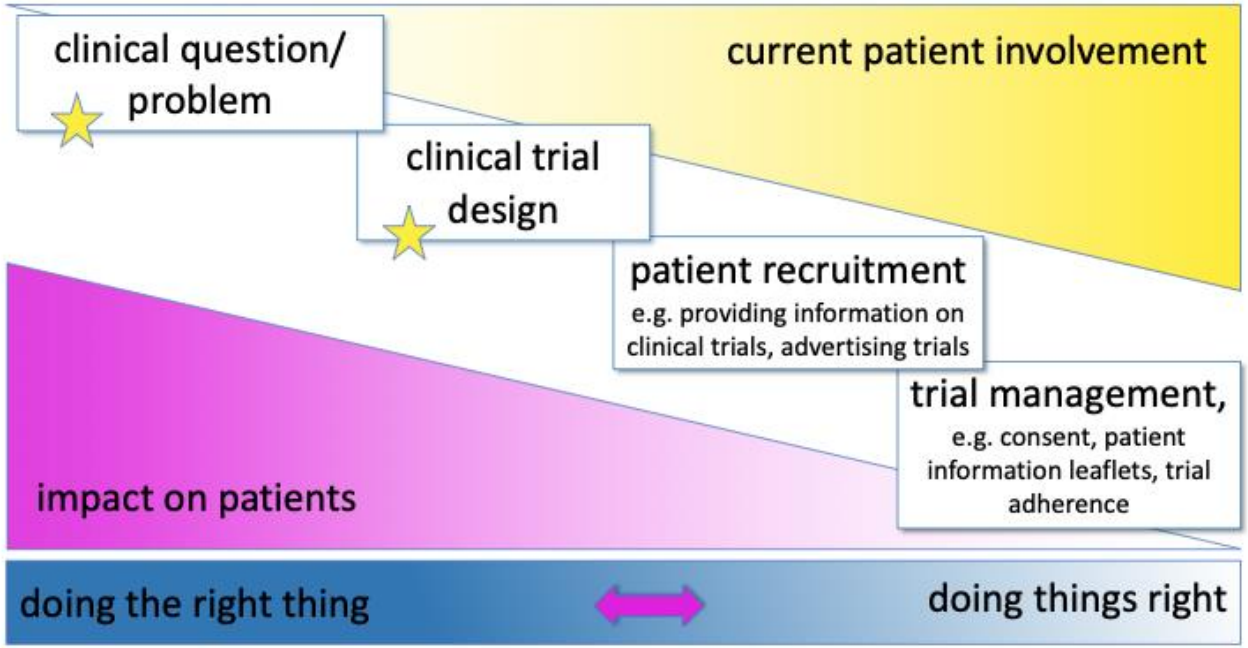
Quality not Quantity.
We need BETTER trials.

The strategy piece

Return on Engagement

Patient involvement in clinical trial design



http://www.informed-scientist.org/presentation/the-role-of-patient-groups-in-the-clinical-trial-process

B. RYLL

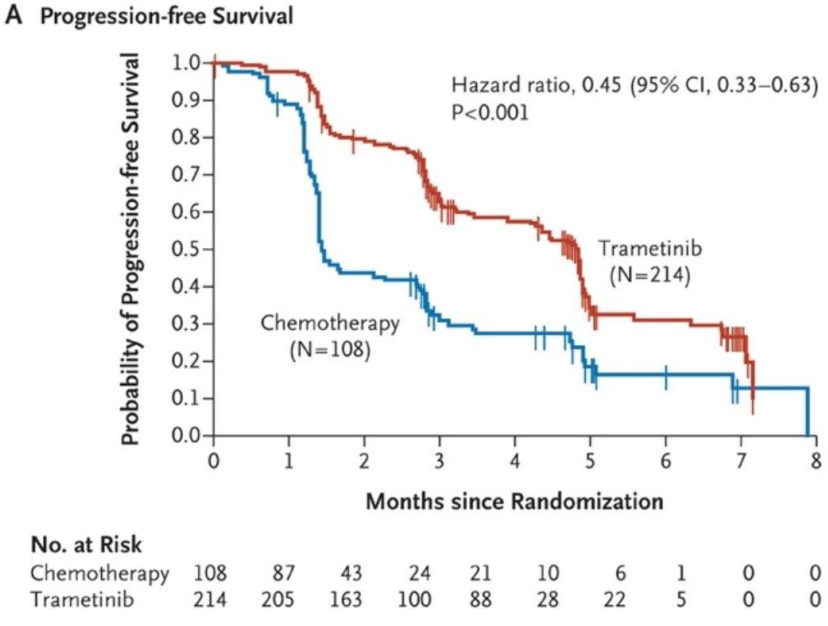
the real issues

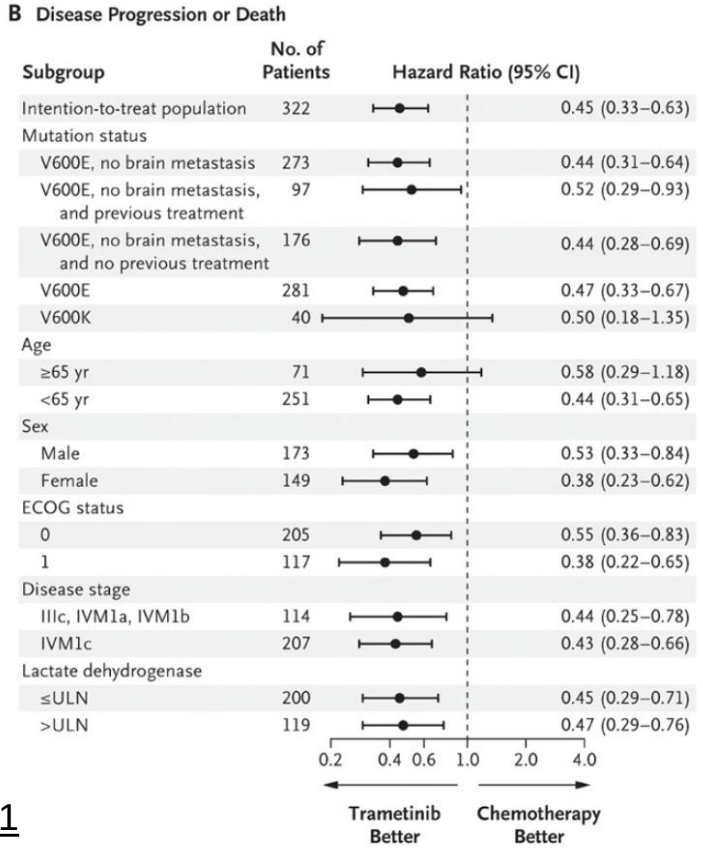
MPNE

B.Ryll, MD/PhD 5th July 2019

Some substance

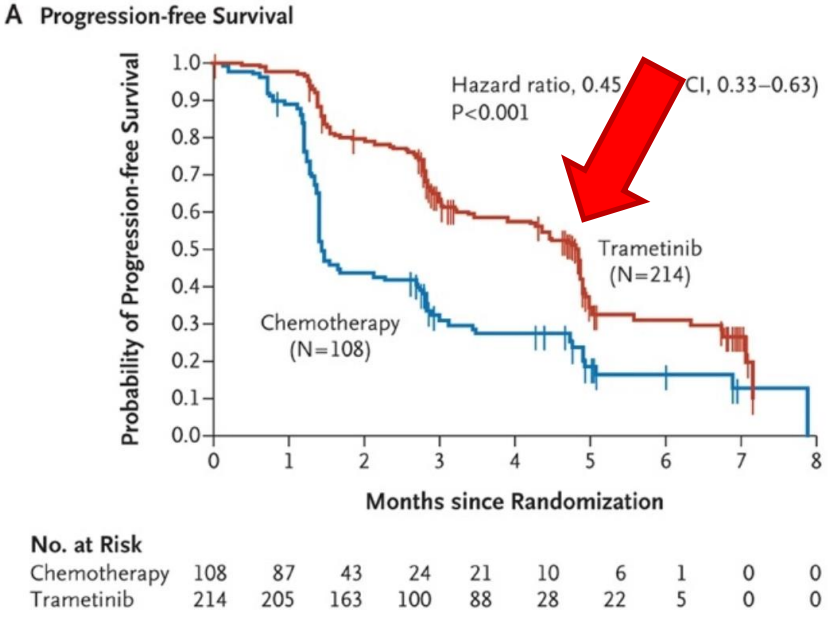
Why I care

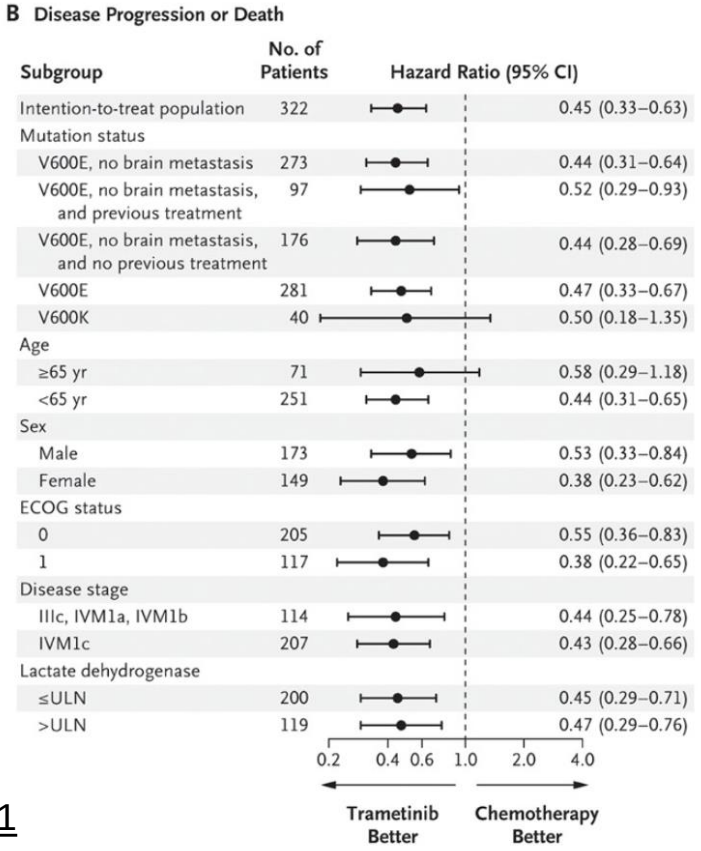




https://www.nejm.org/doi/full/10.1056/NEJMoa1203421

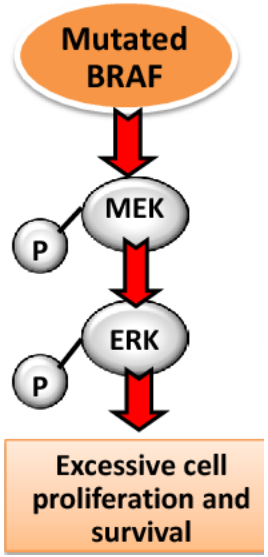
Why I care





https://www.nejm.org/doi/full/10.1056/NEJMoa1203421

Scientific reasoning



- BRAFmut Melanoma depends on activated BRAF pathway
- BRAF works better than DTIC
- MEK works better than DTIC
- BRAF works better than MEK
- BRAF+ MEK works best

- We got 3 BRAF+ MEK combinations.
- DTIC old standard of ~~care~~ desperation, dirt- cheap.

- Which trial design would you want to see?
- Which trial design do you think you will get?

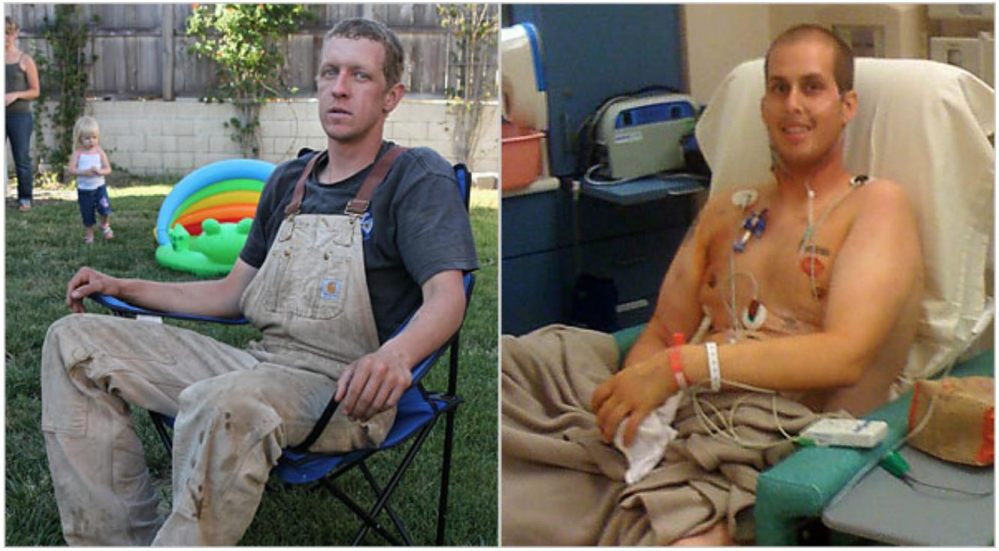
What we got

- Vem vs DTIC 2011
- Dab vs DTIC 2012
- Tram vs DTIC 2012
- Vem + Cobi vs Vem + **placebo** 2014
- Dab + Tram vs Vem 2015
- Enco vs Enco+ Bini vs Vem 2018

- BRAF inhibitors
- MEK inhibitiors

New Drugs Stir Debate on Rules of Clinical Trials

By **AMY HARMON** SEPT. 18, 2010



Two Cousins, Two Paths Thomas McLaughlin, left, was given a promising experimental drug to treat his lethal skin cancer in a medical trial; Brandon Ryan had to go without it.

Monica Almeida/The New York Times, left

RELATED C

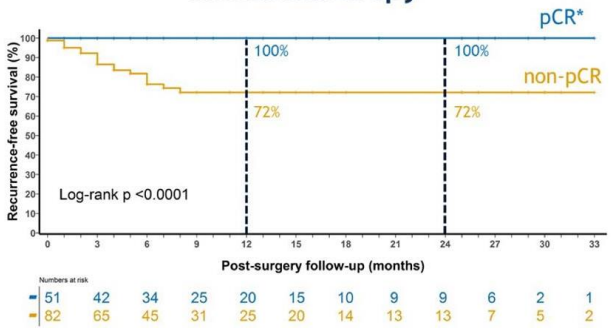
CONSULTS

Ask an E

https://www.nytimes.com/2010/09/19/health/research/19trial.html

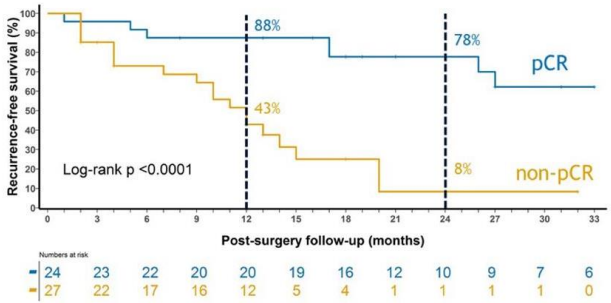
RFS by pathological response and drug

Immunotherapy



Med f/u 10 mo

Targeted Therapy



Med f/u 22 mo

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

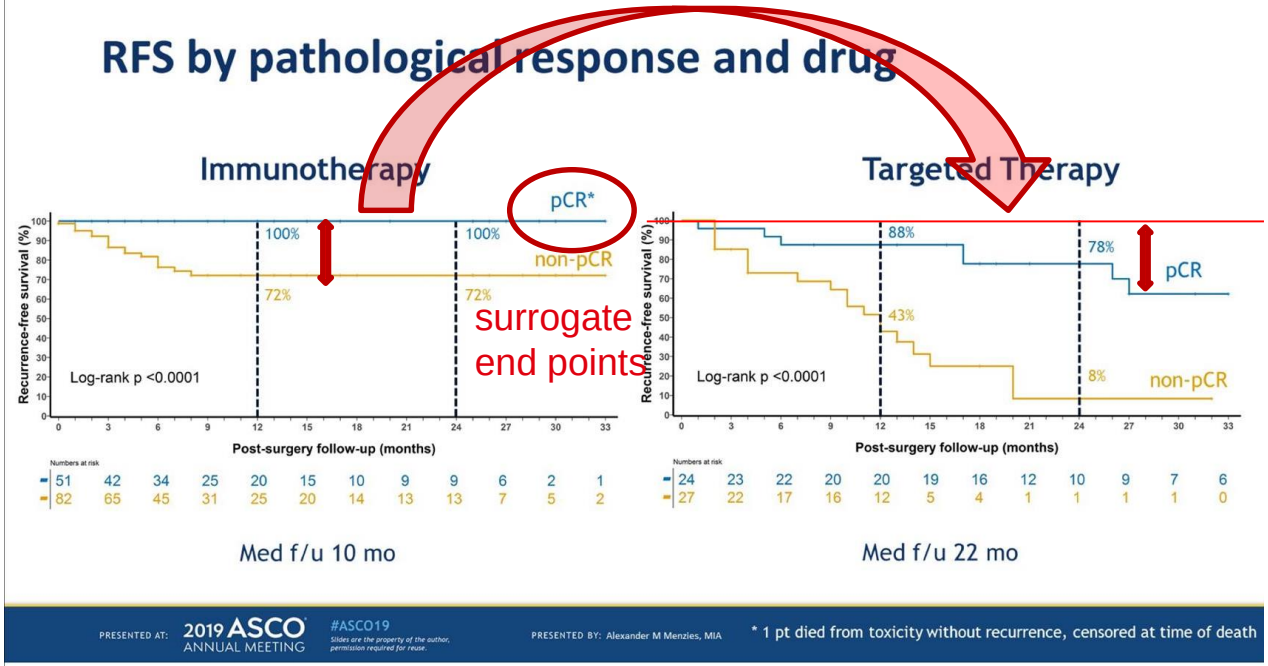
PRESENTED BY: Alexander M Menzies, MIA

* 1 pt died from toxicity without recurrence, censored at time of death

Presented By Alexander Menzies at 2019 ASCO Annual Meeting

mechanism

next trial design?



surrogate end points

Presented By Alexander Menzies at 2019 ASCO Annual Meeting

The trials we don't want

Scientifically unsound.
Helsinki violations.
Inferior comparators.
Trial design not in patient's best interest.
Treatment effect large but still randomised.
You wouldn't go on this trial either!

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The trials we don't want

S cientifically unsound.
H elsinki violations, esp Art 8 and Art 26.
I nferior comparators.
T rial design not in patient's best interest.
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Y ou wouldn't go on this trial either!

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Summary

- Clinical trials offer treatment options for patients who have no other option left
- If we want a better future for our patients, we need research
- Not all research is good- the normal distribution also applies here
- Finding, selecting and shaping research requires expertise
- Research takes time – favour long-term engagement and interaction with research groups and- no short-cut to knowledge.
- Know where to target your efforts
- Know your non-negotiables

Take home

- **Trials that don’t recruit get amended.**
- **Don’t support research you haven’t read or that you don’t understand.**

Thank you for listening

- bettina.ryll@mpneurope.org