UNIVERSITY OF HAWAI'I
CANCER CENTER

Emerging Therapies and Access Issues in Hawaii: Phase I Trials

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10-17-2020

1

Outline

- Modern vs. traditional phase I trials
- Impact of phase I trials for cancer patients
- Timelines from discovery to phase I to adoption
- Update on UHCC-HCC phase I trials initiative
- Nursing considerations for early phase clinical trials

2

2

Definitions – Phase I trials

Traditional	Modern
• Dose-finding studies with cytotoxic drugs	• Targeted agents on well-defined cancer sub-populations
• Dose escalation until no longer tolerable	• Focus to understand drug activity
• Broad patient eligibility	• Dose escalation may not be a feature
• Safety and toxicity endpoints	• Response rates are ~20-40%
• Anticipate ~5% response rate	• 20-1000 patients
• 20-50 patients	◦ Keynote 001 (1200 patients)

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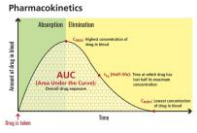
Definitions – Phase 0 trials

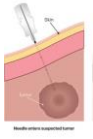
Traditional

- Pharmacokinetics
- Understand distribution of drug within human systems



Modern

- Define and confirm tumor target effects
- Often involves on-treatment, sequential tumor biopsies
  - Potential to use "liquid biopsies"



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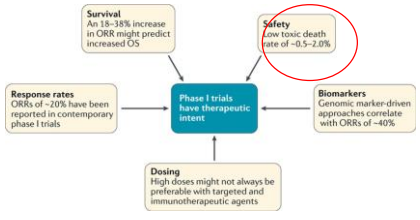
New phase 1 paradigms



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Impact of phase 1 trials for cancer patients

- Early phase trial are increasingly including efficacy endpoints and large expansion cohorts
- Molecularly targeted subgroups allows for therapeutic intent, even in "first-in-human" studies
- FDA may approve drugs for clinical use based on phase I study results
  - Ceritinib for ALK-rearranged NSCLC
  - Pembrolizumab for melanoma

6

6

Cautionary notes for EPCT

- Molecularly targeted subpopulations can markedly improve response rates but may narrow eligibility to a small percentage of patients with a particular cancer.
- Most phase I trials have fairly strict "performance status" requirements so patient enrollment following progression on standard therapy, but before multiple rounds of ineffective salvage regimens, is desirable.
- Immunotherapy benefits on OS, without appreciable impacts on ORR, complicate end point considerations for phase I trials with these agents.

7

7

Ethical considerations for Hawaii

- Cancer patients who feel reasonably "well" despite having progressed on standard therapies often want the hope that EPCT provide.
  - Need to balance this with realistic expectations
- Access to EPCT is difficult and expensive for Hawaii patients until we have a program based here in the state.
- Financial Considerations – most trial costs are covered but often not transportation, housing, missed work & other living expenses if patients need to travel outside of Hawaii.

8

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Ethical considerations for Hawaii

- Most patients who enroll on EPCT are affluent and from urban areas with large academic medical centers.
- Most patients who enroll on EPCT are white.
  - Very important to define if new agents have efficacy in other populations like those in Hawaii.

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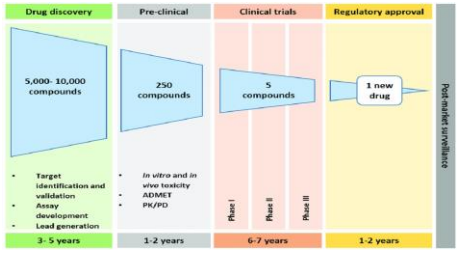
Cancer drug development timeline



11-16 years!

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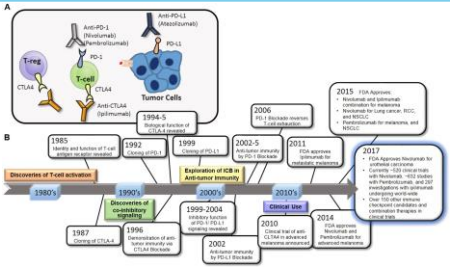
Timeline for development of checkpoint inhibitors (αPD-1; αPD-L1)



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Currently in design phase. Permitting and buildout anticipated for 2021.

13

13