Real World Evidence in Oncology and its Implications

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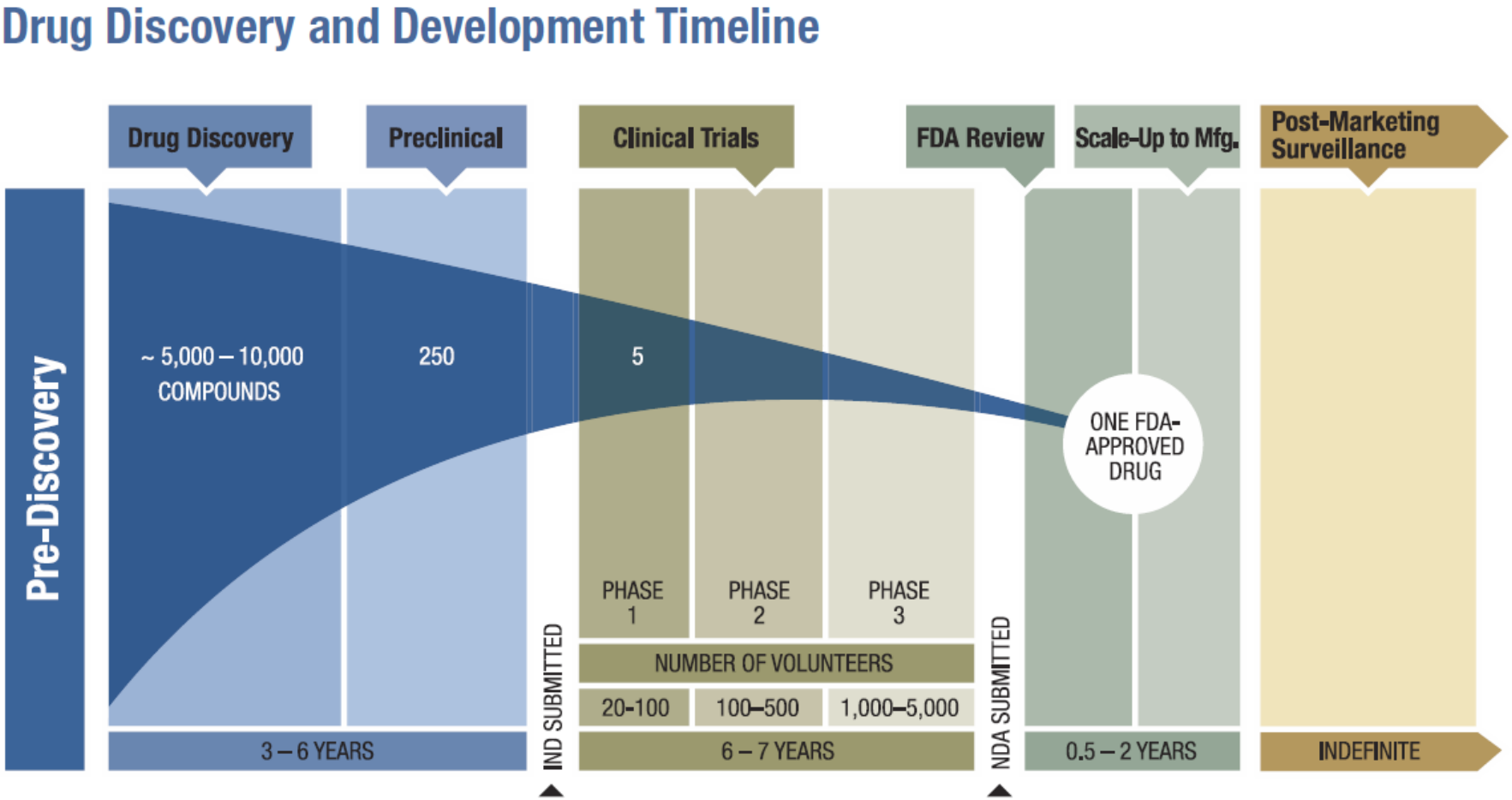
Traditional Drug Development Paradigm



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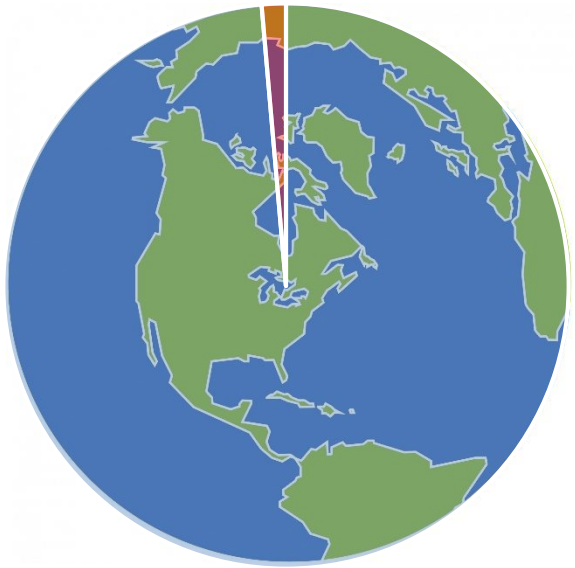
Real World Evidence is Vast

- **Real-World Data (RWD)** is data collected from sources outside of traditional clinical trials. These sources may include large simple trials, or pragmatic clinical trials, prospective observational or registry studies, retrospective database studies, case reports, administrative and healthcare claims, electronic health records, data obtained as part of a public health investigation or routine public health surveillance, and registries (e.g., device, procedural, or disease registries). The data is typically derived from electronic systems used in health care delivery, data contained within medical devices, and/or in tracking patient experience during care, including in home-use settings.

- **Real-World Evidence (RWE)** is the evidence derived from aggregation and analysis of RWD elements.

"(b) REAL WORLD EVIDENCE DEFINED.—In this section, the term 'real world evidence' means data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than randomized clinical trials.



***Among 20,929 interventional clinical trials conducted between 2007 and 2016 that had the primary purpose of evaluating one or more cancer drugs, 7,248, or 34.6% incorporated randomized allocation into their study design.

~ 1.38% CT ; 98.62% RWE

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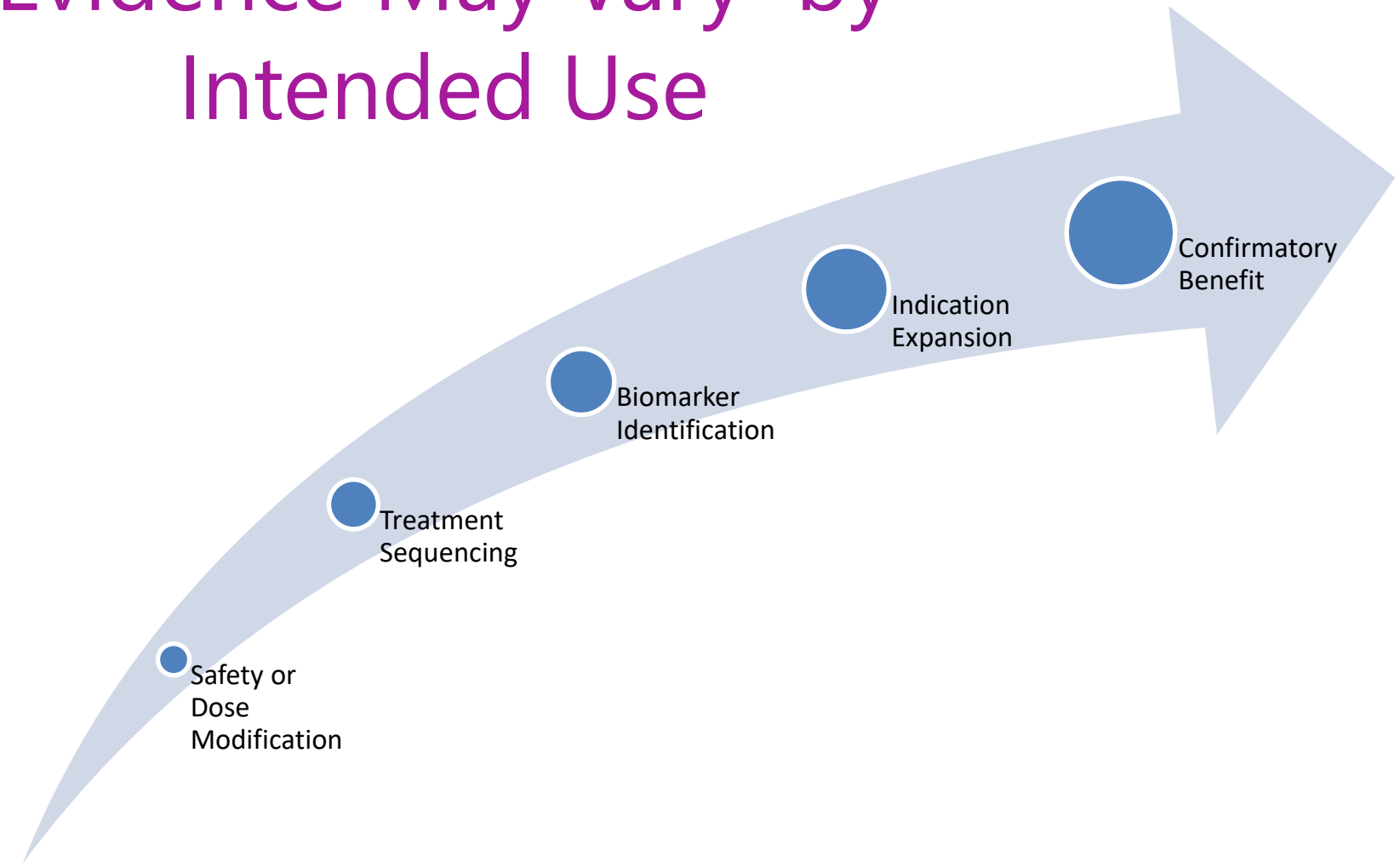
Evidence May Vary by Intended Use



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Incorporating RWE into Practice

- **Growing interest in use of RWE for "regulatory decision making"**
- **Given the diversity of evidence, is there a role for a neutral entity to assess the quality of evidence?**
- **Opportunities for communicating high-quality RWE – the FDA product label**
  - FDA-approved labels should be a vitally important source of information to guide the safe and effective use of prescription drugs.
  - One half and three quarters of all oncology prescribing is done off label.[1]
  - 27% of off-label uses were backed by strong evidence, with the remaining uses lacking strong scientific support.[2]

- **<u>Question</u>: Is there a subset of RWE that would be regarded as high-quality, medically accepted information that should be incorporated into product labels over time?**

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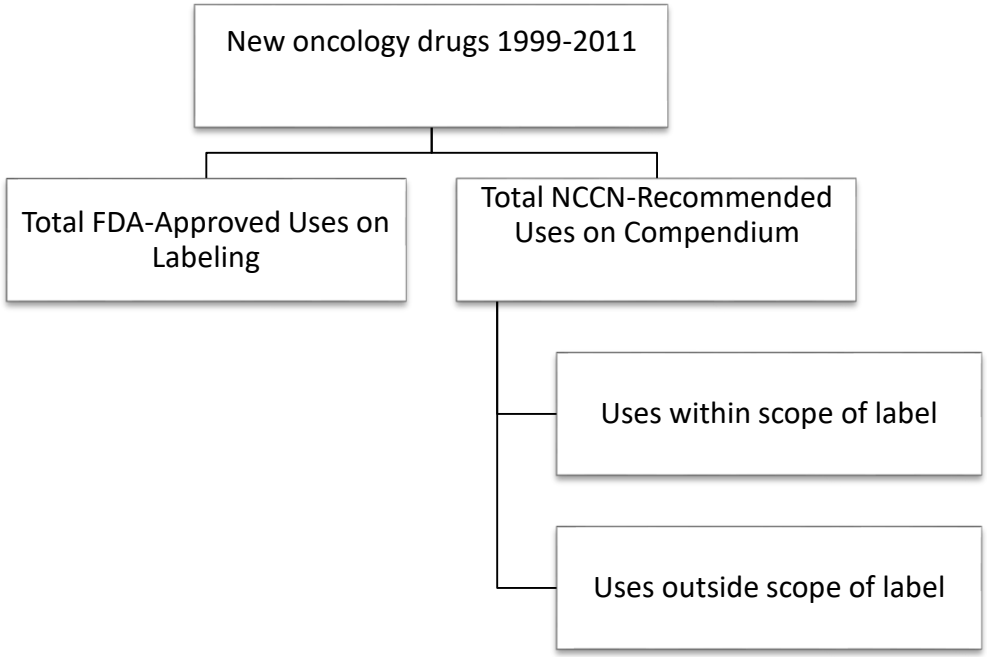
[1] Mullins CD, Montgomery R, Abernethy AP, Hussain A, Pearson SD, Tunis S; American Society of Clinical Oncology. Recommendations for clinical trials of off-label drugs used to treat advanced-stage cancer. J Clin Oncol. 2012 Feb 20;30(6):661-6.

[2] Radley D, Finkelstein S, Stafford R. Off-label Prescribing Among Office-Based Physicians. Arch Intern Med. 2006 May 8;166(9):1021-6.

Use of RWE to Date

- To assess how evolving post-market evidence is incorporated into product labels, we compared treatment guidelines developed by expert oncologists to current FDA approved labels
- The sample period was chosen to allow time for additional evidence to be developed post-approval (>5 years)



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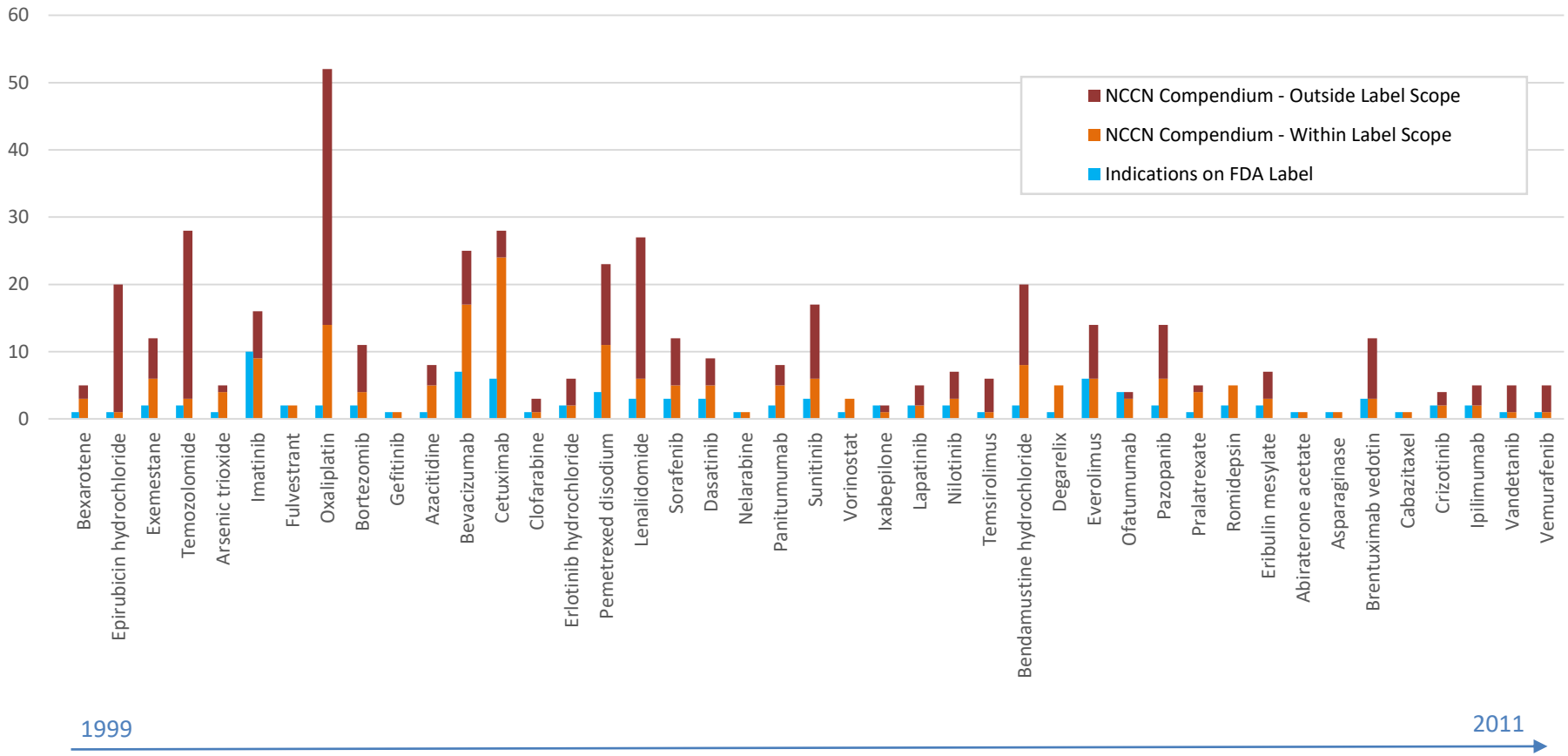
Use of RWE to Date



NOTES The number of indications listed on FDA-approved labeling was compared to uses recommended in the NCCN Drug and Biologics Compendium. The NCCN Compendium is often much more specific than FDA labeling, leading to many uses being listed without necessarily going outside the scope of the label. Drug uses listed on the NCCN Compendium were categorized as either within or outside the scope of FDA labels. Drug uses categorized outside the scope of the label were considered to be off-label uses.

Incorporating RWE into Practice

- In almost every case (34 of 43; 79%), the NCCN compendium had more recommended uses than those described in the FDA label for the drugs analyzed in this study
- Of the 450 NCCN-recommended uses associated with all drugs included in the study, 253 (56.3%) were outside the scope of the FDA label
- Additionally, 65% of the off-label uses in the NCCN Compendium represented new disease indications, meaning these uses were in disease settings not currently represented on FDA-approved labels.
- 91% of off-label uses were graded as NCCN Category 1 or 2A, indicating they are backed by uniform consensus from NCCN advisory committees, and thereby recognized as acceptable uses by the 4 largest private insurers

Conclusions

- Currently, sponsors can submit a supplemental new drug application to modify a product label with additional efficacy claims.
- However, there may be instances when the efficacy profile of a drug has evolved but no supplemental application to the label was ever submitted.
- This typically happens when incentives to submit additional information are limited, such as when a drug has gone off patent and faces generic competition, or when a drug is no longer actively marketed.
- The FDA could play a greater role in evaluating the relevant data to update the product label, as appropriate, and adjudicate between uses backed by strong evidence and those backed by less persuasive information.
- This would establish a high standard for post-market evidence and make product labels more useful.