# Assessing the Financial Value of Patient Engagement: A Quantitative Approach from CTTI's Patient Groups and Clinical Trials Project

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## Supplement S2. Base Case Details

This appendix presents technical risks, development costs, and development times for the base case—a typical clinical development program for an oncology indication.

### Technical Risks

A recent study of oncology drug development by the Tufts Center for the Study of Drug Development (CSDD) provides estimates of technical risks by phase for new oncology drugs.[41] Technical risk is defined as the probability that a single indication for a compound will transition from one phase to the next (**Table S2-1**).

**Table S2-1. Technical Risks for Lead Indications of Investigational Oncology Drugs and Biologics First Entering the Development Worldwide (1993-2004)[a]**

| Development Phase | Technical Risk (Probability of Transition to Next Phase) | Probability of Technical and Regulatory Success |
|---|---|---|
| Phase 1 | 59.4% | 9.0% |
| Phase 2 | 33.0% | 15.1% |
| Phase 3 | 52.4% | 45.9% |
| Regulatory Review | 87.5% | 87.5% |

[a]Self-originated compounds in the pipelines of top 50 pharmaceutical firms (by sales in 2006).

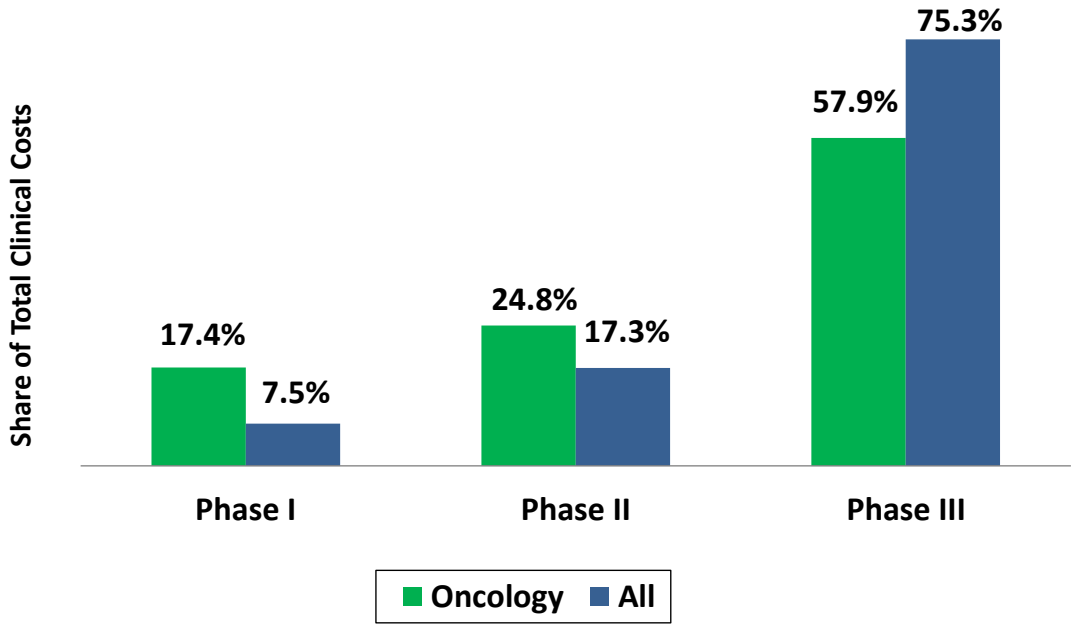
The product of these probabilities from a given phase through regulatory review gives the probability of technical and regulatory (PTRS) success for that phase. For example, for a lead oncology indication in phase 1, PTRS is 9.0%.

**Development Costs**

Trial cost benchmarks are generally reported at the molecule level and cannot be used directly for analyses at an indication level.[42] We use ratios of cost per phase derived from such data, coupled with the average number of indications studied per phase, to estimate costs by phase at an indication level. [42]

A recent CTTI/Tufts CSDD study showed $69,000 cost per patient and 448 patients for a typical phase 3 oncology trial, yielding a cost per trial of $30,912,000.[43] **Figure S2-1** shows relative mean phase costs associated with each phase for oncology drugs and for drugs in general (calculated using data collected for a Tufts CSDD study of R&D costs.[42]) The shares are nearly identical if median costs are used.

**Figure S2-1. Distribution of Clinical Period Costs by Clinical Phase**




These costs include multiple indications, and the number of indications pursued is not constant across phases. In general, we expect more indications in early phases than later due to attrition. Complicating matters for oncology drugs is that they tend to be pursued in many more indications than is the case for non-oncology drugs.[42] Phase 1 testing in oncology is often not distinguished by indication (this is much less true for non-oncology drugs); instead, indication-specific trials for oncology drugs are often initiated in phase 2. There is also less information in the cost dataset on oncology drugs than for drugs as a whole. For these reasons, we use shares for all drugs rather than for oncology drugs and adjust them based on other the number of indications pursued. Note that this assumes that relative costs across phases for a given indication are the same for oncology drugs as they are for all drugs. For drugs as a whole, for drugs terminated in phase 1, an average of 1.41 indications were studied; for drugs terminated in phase 2, an average of 1.94 indications were examined (the latter average may overstate

somewhat the number of indications pursued in phase 2 as some of these indications may have been examined only in phase 1). Adjusting the cost shares by these averages gives estimates for relative phase costs per indication (**Table S2-2**).

**Table S2-2. Phase 1 and Phase 2 Costs Relative to Phase 3 Costs**

| | Cost Share Relative to Phase 3 | Cost Share Relative to Phase 3 Adjusted by Number of Indications |
|---|---|---|
| Phase 1 | 10.0% | 7.1% |
| Phase 2 | 23.0% | 11.8% |

The benchmark phase 3 cost results above together with the relative cost shares and an assumption about how many phase 3 trials are conducted can be used to infer clinical phase costs (**Table S2-3**).

**Table S2-3. Estimate for Clinical Costs by Phase for an Oncology Indication Using Relative Phase Costs**

| | Cost Relative to Phase 3 | Phase Cost |
|---|---|---|
| Phase 1 | 7.1% | 0.071 * $69,000 * N * T |
| Phase 2 | 11.8% | 0.118 * $69,000 * N * T |
| Phase 3 | 100% | $69,000 * N * T |

N=number of subjects in a phase 3 trial; T=number of phase 3 trials conducted.

Thus, assuming two phase 3 registration trials are conducted with 448 subjects in each, the phase 1, 2, and 3 costs are $4.4 million, $7.3 million, and $61.8 million, respectively.

**Development Times**

The Tufts CSDD database of approved small molecules and biologic compounds provides average total U.S. clinical phase times by therapeutic class in the United States from 2000 to 2014.[45] The mean clinical phase time for antineoplastics is 88.8 months, and the mean regulatory review time is 9.6 months. Since this dataset does not have times for individual development

phases, we used the Tufts CSDD R&D cost study for this information. However, as the number of oncology drugs in the R&D cost dataset is limited, we assess phase times for all drugs in the dataset taken as proportions of total clinical time, then apply these proportions to the total clinical time of 88.8 months (**Table S2-4**). Note that using the actual times available for oncology drugs in the R&D cost study dataset would make little difference. The sum of the mean phase times for oncology drugs in that dataset [89.3 months] is nearly identical to the estimate of total time for the 2000 to 2014 approvals. In addition, the shares of total time by clinical phase are close to those for drugs in general in the R&D cost study dataset. Note also that phases are assumed to take place successively even though phases can overlap somewhat in actuality. Since the shift in costs that this assumption entails is on the order of a few months to a year, but the total cost is unchanged, the impact of this assumption on ENPV assessments is minimal.

**Table S2-4. Clinical Phase and Regulatory Review Times for Lead Oncology Drugs**

| | Phase Times for All Drugs (months)[42] | Share of Total Clinical Time for All Drugs | Calculated Phase Times for Oncology Drugs (months)[a] |
|---|---|---|---|
| Phase 1 | 19.8 | 24.5% | 21.8 |
| Phase 2 | 30.3 | 37.5% | 33.3 |
| Phase 3 | 30.7 | 38.0% | 33.7 |
| Regulatory Review | 16.0 | --- | 9.6 |

[a]Uses average time from IND filing to NDA/BLA submission of 88.8 months and regulatory review time of 9.6 months for new oncology drugs approved in the United States from 2000 to 2014.[45]