**Research Plan**

**Part I: Investigate the impact of the basket trial on the success of the subsequent phase 2 trials. (Similar ideas to Kasim et al., 2023)**

1. Simulation procedures:

* Step 1: generate phase 1b data.
* Step 2: conduct analysis on data from step 1 using methods of interest.
* Step 3: calculate empirical success rates from phase 1b trial and phase 2 trial.
* Step 4: calculate the mean square errors for the estimated response rate.

1. Simulation scenarios

* Homogeneity vs heterogeneity.
* Number of baskets.
* Basket sizes.
* Binary outcomes (e.g., ORR), survival outcomes (e.g., PFS), continuous.

**Part II: Optimize the decision criteria for the success of the subsequent phase 2 trials (based on promising methods identified in Part I).**

1. Fix sample size (determined by budget).
2. Minimize type I and type II error rates at phase 2 (theoretical derivations or computational approaches).

**Comparison of statistical methods:**

*Selection criteria: (1) outcome types, (2) available software, (3) can be used for both design and analysis.*

Binary outcome:

1. Simon (1989): <https://doi.org/10.1016/0197-2456(89)90015-9>
2. Thall et al. (2003): <https://doi.org/10.1002/sim.1399>
3. Berry et al. (2013): <https://doi.org/10.1177/1740774513497539>
4. Chen et al. (2016): <https://doi.org/10.1080/19466315.2016.1193044>
5. Neuenschwander et al. (2016): <https://doi.org/10.1002/pst.1730>
6. Simon et al. (2016): <https://doi.org/10.1053/j.seminoncol.2016.01.002>
7. Cunanan et al. (2017): <https://doi.org/10.1002/sim.7227>
8. Chu et al. (2018a): <https://doi.org/10.1177/1740774518755122>
9. Chu et al. (2018b): <https://doi.org/10.1111/rssc.12255>
10. Hobbs et al. (2018): <https://doi.org/10.1002/sim.7893>
11. Asano et al. (2020): <https://doi.org/10.1002/pst.2049>
12. Chen et al. (2020): <https://doi.org/10.1177/0962280220910186>
13. Jin et al. (2020): <https://doi.org/10.1002/sim.8675>
14. Jiang et al. (2021): <https://doi.org/10.1016/j.cct.2021.106460>
15. Psioda et al. (2021): <https://doi.org/10.1093/biostatistics/kxz014>
16. Liu et al. (2022): <https://doi.org/10.1002/sim.9514>
17. Zabor et al. (2022): <https://doi.org/10.1177/17407745211073624>

Survival outcome:

1. Chen et al. (2016): <https://doi.org/10.1080/19466315.2016.1193044>
2. Palmer et al. (2020): <https://doi.org/10.1016/j.cels.2020.09.003>
3. He et al. (2022): <https://doi.org/10.1177/09622802221091901>
4. Pan et al. (2022): <https://doi.org/10.1080/10543406.2022.2089160>

Continuous outcome:

1. Chen et al. (2016): <https://doi.org/10.1080/19466315.2016.1193044>
2. Chu et al. (2018b): <https://doi.org/10.1111/rssc.12255>
3. Jin et al. (2020): <https://doi.org/10.1002/sim.8675>
4. Palmer et al. (2020): <https://doi.org/10.1016/j.cels.2020.09.003>
5. Zheng et al. (2022): <https://doi.org/10.1093/biostatistics/kxaa019>

**Bayesian hierarchical models**

**Variations under exchangeability assumption:**

1. *Thall et al. (2003):* [*https://doi.org/10.1002/sim.1399*](https://doi.org/10.1002/sim.1399) *[analysis, binary + survival]*

* **Method:** under exchangeability assumption with user specified priors (data model + parameter model)
* **Software:** WinBUGS code available in the main text (run WinBUGS code in R: Sturtz et al. (2005): <https://www.jstatsoft.org/article/view/v012i03>)

1. *Berry et al. (2013):* [*https://doi.org/10.1177/1740774513497539*](https://doi.org/10.1177/1740774513497539)

* Same approach as Thall et al. (2003)

1. *Cunanan et al. (2017):* [*https://doi.org/10.1002/sim.7227*](https://doi.org/10.1002/sim.7227)

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1. *Lin et. al. (2021):* [*https://doi.org/10.1214%2F20-ba1205*](https://doi.org/10.1214%2F20-ba1205)

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**Approach 1 to relax the exchangeability assumption: EXNEX model and its variations**

1. *Neuenschwander et al. (2016):* [*https://doi.org/10.1002/pst.1730*](https://doi.org/10.1002/pst.1730) *[analysis, binary]*

* **Method:** basket assumed to be exchangeable with a user-specified probability (exchangeable → common parameter model; non-exchangeable → basket-specific parameter model)
* **Software:** WinBUGS code available in the supplementary materials

1. *Chen et al. (2023):* [*https://doi.org/10.1002/pst.2289*](https://doi.org/10.1002/pst.2289) *[analysis, binary]*

* **Method:** basket determined to be exchangeable or non-exchangeable depending on some decision criteria (data-dependent EXNEX/DEXNEX)
* **Software:** NA

**Approach 2 to relax the exchangeability assumption: Testing for homogeneity**

1. *Liu et al. (2017):* [*https://doi.org/10.1016/j.cct.2017.06.009*](https://doi.org/10.1016/j.cct.2017.06.009)

* **Method:** two decision points: (1) test for homogeneity (yes → (2), no → Simon’s two-phase design); (2) test for futility for each basket (low power → stop enrollment, not low power → Bayesian hierarchical mixture model). Cutoffs at two decision points and sample sizes are optimized by simulation.
* **Software:** NA

1. **cc**

**Approach 3 to relax the exchangeability assumption: Clustering**

* **Simon’s two stage design**
* **BHM (half-normal prior, inverse gamma prior**
* **EXNEX**
* **BHMM**
* **Calibrated BHM**
* **BLAST**
* **Simon’s Bayesian basket design**
* **Cunanan two-stage design**