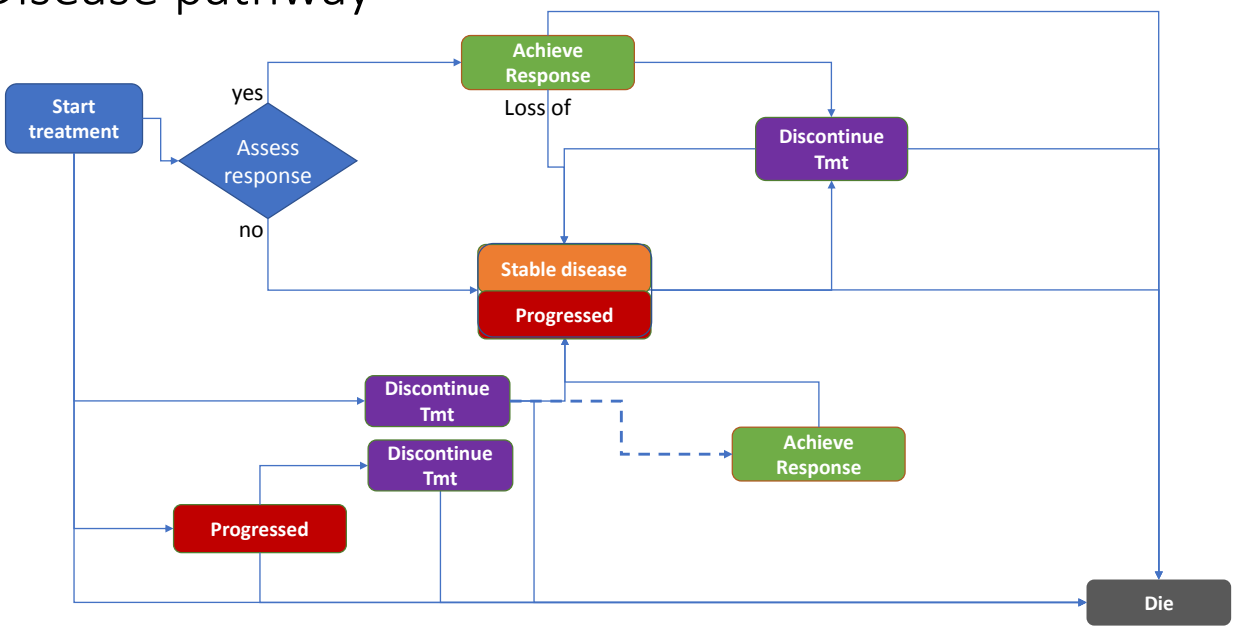
Modelling Response

Jaime Caro

Model Structures Incorporating Response

1. Partitioned Survival Analysis
   A. Modified With Response
   B. With Landmark Analysis
2. Time-to-Event

Disease pathway

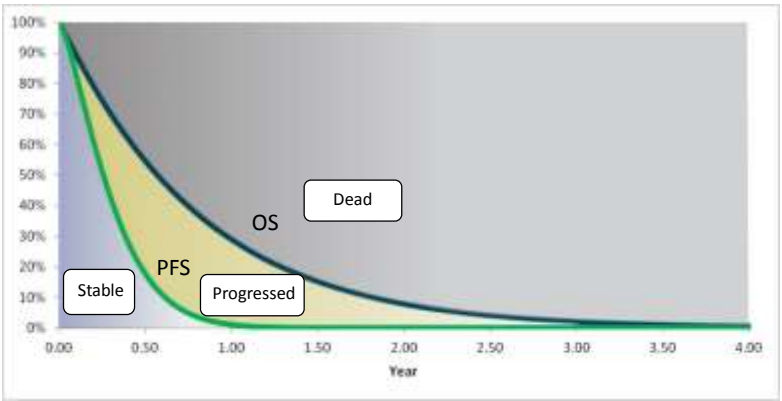


Partitioned Survival Analysis: Classic

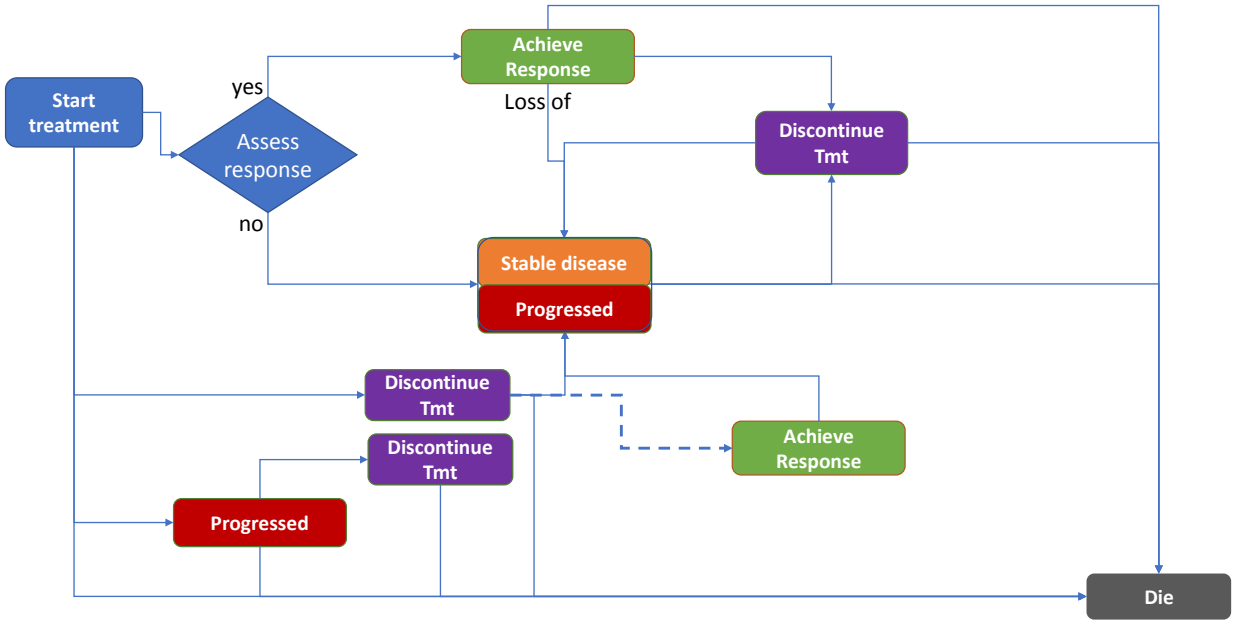
- Most common modeling technique in oncology
- Well received by HTAs and clinicians and easy and quick to implement
- Based on the historically most common clinical trial outcomes: OS and PFS

Underlying assumptions:

- Costs, utilities and survival depend on progression status
- Treatment costs often external to structure with time-to-treatment discontinuation curves.

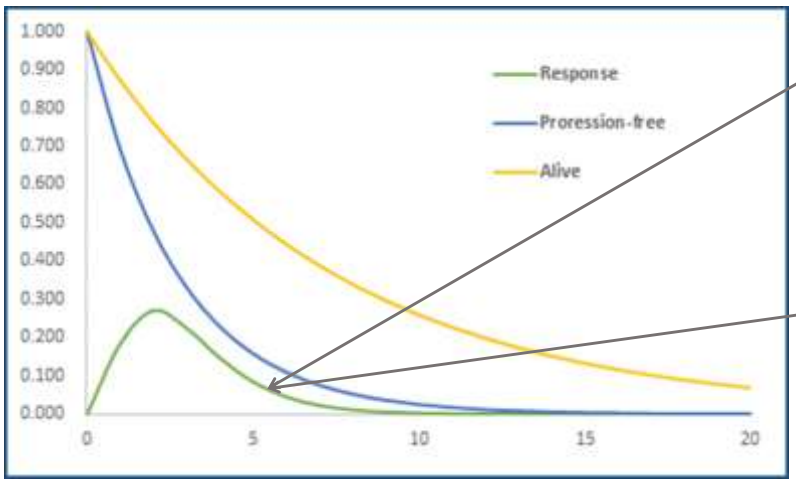


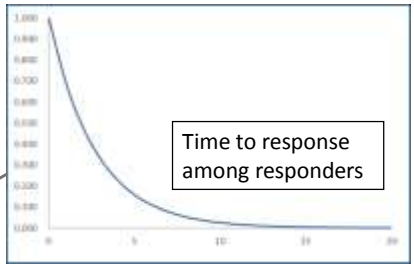
Disease pathway very limited with partition SA



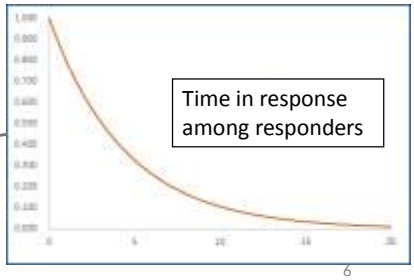
1A. Partitioned Survival Analysis: With Response

- Accepted structure with the use of response
- Can be extrapolated
- Data are often available
- Treatment costs often external to structure



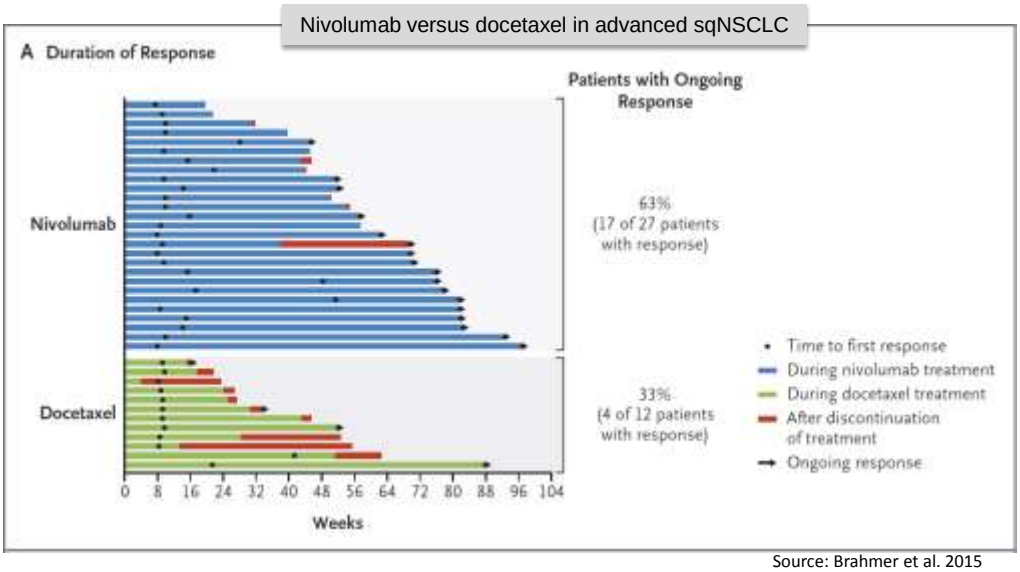


Time to response among responders



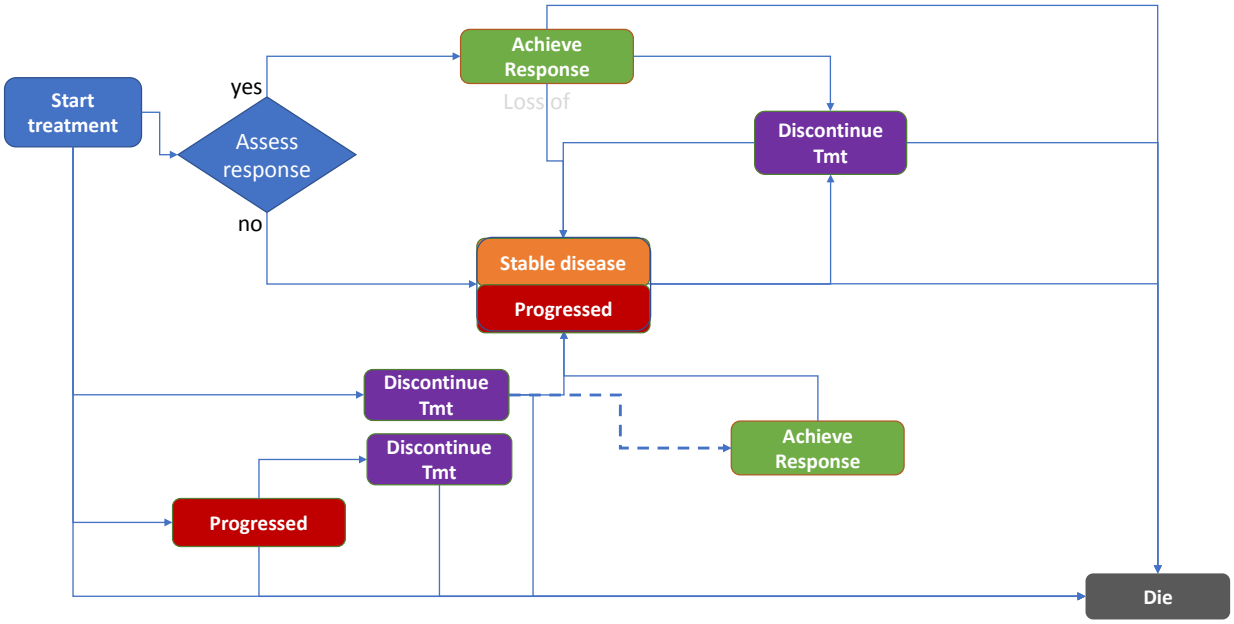
Time in response among responders

Example of Data for Modified Partitioned SA

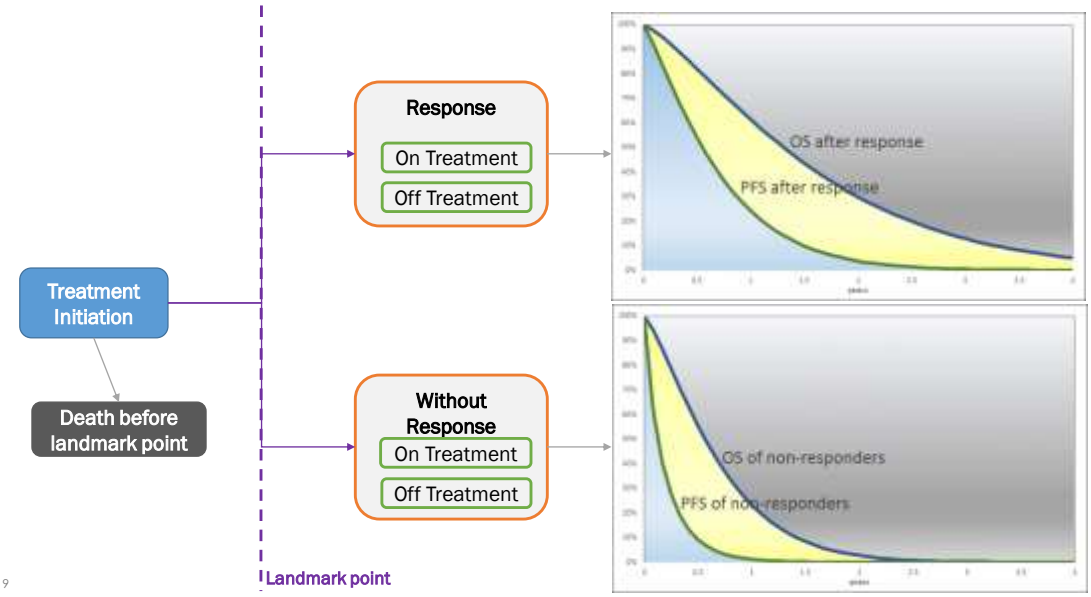


Source: Brahmer et al. 2015

Disease pathway still limited with response



1B. Partitioned Survival Analysis with Landmark Analysis



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Partitioned Survival Analysis with Landmark Analysis

Advantages

- Allows modelling survival according to response
- Might be easier to fit survival, if it follows simpler patterns conditional on response
- Still simple and easy to understand
- Better clinical validity
- Keeps the partitioned survival structure

Disadvantages

- Choice of landmark point is subjective
- Results of clinical trials are rarely published in this format
- Due to fewer events, extrapolation of OS after response can be even more uncertain
- Potential for bias: patients surviving until landmark point can differ between responders and non-responders

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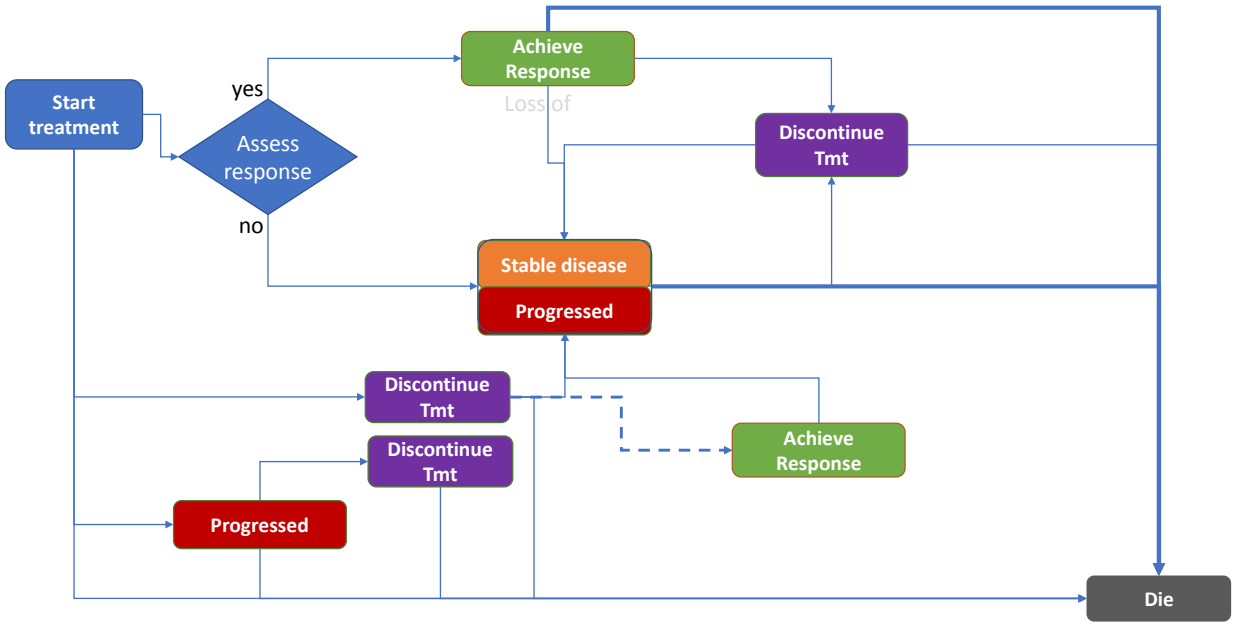
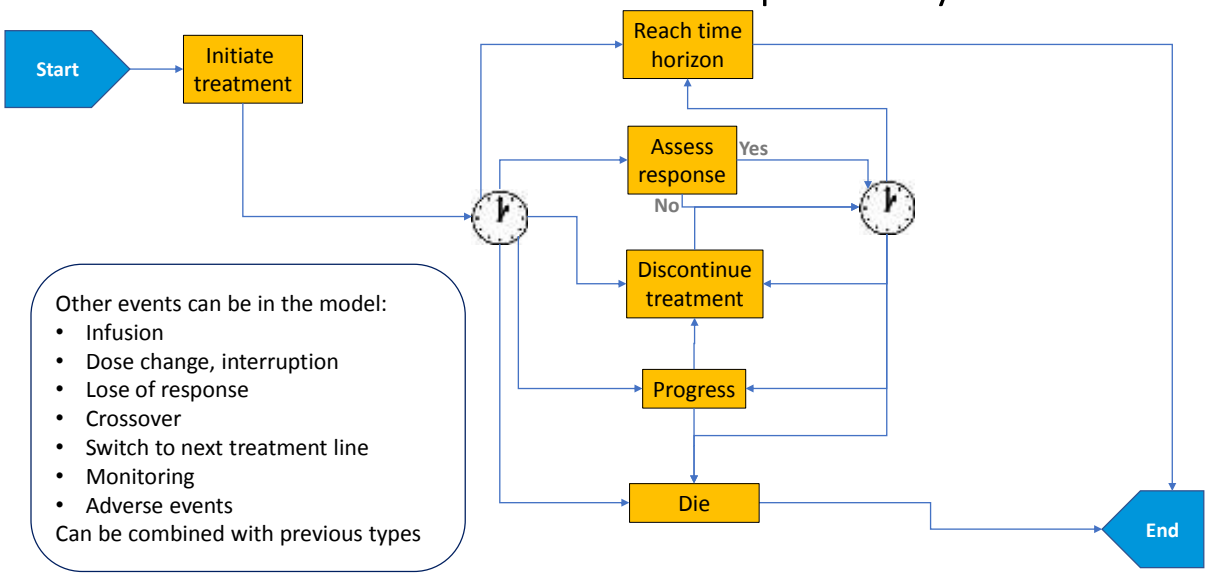
Landmark analysis further extends pathway



2. Time to Event Model – Full pathway



Other events can be in the model:
- Infusion
- Dose change, interruption
- Lose of response
- Crossover
- Switch to next treatment line
- Monitoring
- Adverse events

Can be combined with previous types

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TTE can model the full disease pathway