# Case study

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Acknowledgement:
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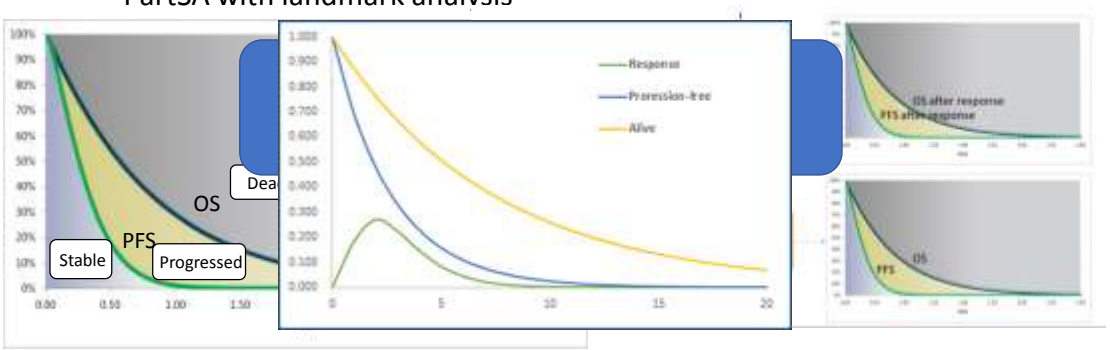
## Aims

- To look at the potential roles of response in oncology in determining cost-effectiveness:
  - No role for response
  - Response influences utilities and disease management costs
  - Response influences survival curves, disease management costs and utilities
  - ~~Response influences survival curves, treatment discontinuation, disease management costs and utilities and allows for response after progression~~
- To evaluate the influence of different inputs and assumptions on the choice of modelling approach

# Model

- Comparators: Immuno-oncology (IO) vs. Chemotherapy
- Three structures in one model
  - Classic partitioned survival analysis (PartSA)
  - PartSA with response
  - PartSA with landmark analysis




# What is DICE?

A modeling technique that conceptualizes the decision-analytic problem in terms of two fundamental aspects:

**Conditions**

- **Aspects that persist over time**
- **Have levels, which can change & affect events**
- **Many conditions can be present at once**
- **Interested in time spent at a given level (value)**

discrete integration

**Events**

- **Aspects that happen at a point in time**
- **Can affect the level of a condition or other events**
- **Many can happen, at any time**
- **Interested in number that happen (and when)**

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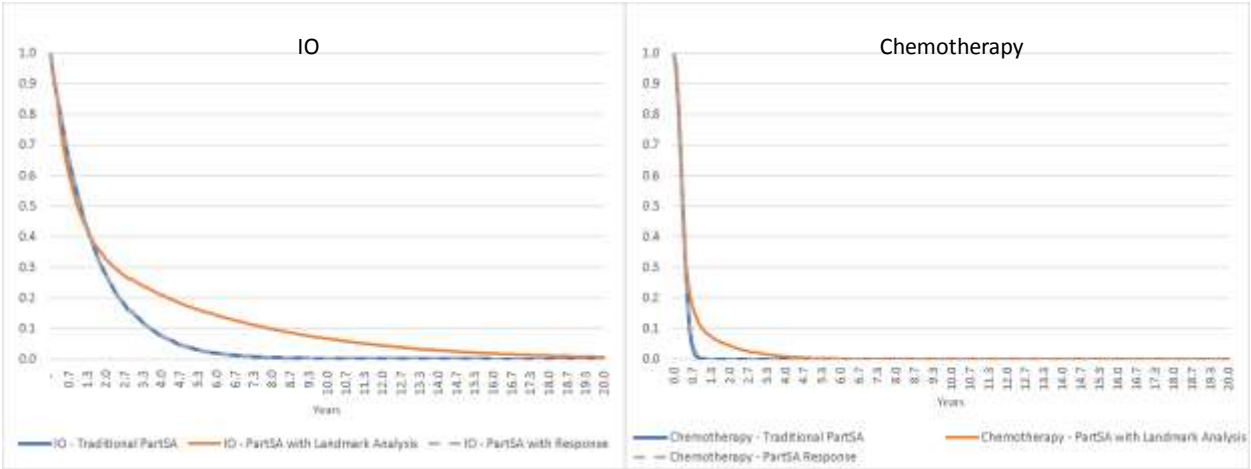
# Inputs: Efficacy and Safety

- Based on a hypothetical patient level dataset
- Extrapolated (where appropriate) using single distributions: Weibull

| | PartSA | PartSA with response | PartSA with landmark analyses |
|---|---|---|---|
| **Survival** | OS (overall) | OS (overall) | OS after response (adjusted UK general population mortality from 70) |
| | | | OS after no response |
| | | | OS (overall) used before landmark |
| **Disease progression** | PFS (overall) | PFS (overall) | Response at landmark (3 months) |
| | | Time to response among responders | PFS after response |
| | | Time in response among responders | PFS after no response |
| **Safety** | Probability of an AE | Probability of an AE | Probability of an AE |

# Extrapolated Overall Survival



# Base Case Assumptions

- Cycle length: one months
- HRs for IO vs. Chemotherapy
  - OS, PFS HRs after response and after no response assumed to be the same for OS (overall)
  - Time to response assumed to be the same for IO and Chemotherapy
- Until landmark point patients are assumed to be Stable
- Utilities
  - Utilities while progression-free, stable and in response assumed to be the same
  - After progression or loss of response utilities decrease
- Costs
  - Costs include: drug (initial and subsequent) and administration costs, monitoring costs, disease management, AE costs
  - Disease management costs while progression-free, stable and in response assumed to be the same
  - Costs after progression and loss of response assumed to be the same
  - Maximum treatment duration 24 months for IO, 6 months for Chemotherapy

# Initial Inputs

| Inputs | IO | Chemotherapy |
|---|---|---|
| HR OS (overall, after response, after no response)# | 0.247 | |
| HR PFS (overall, after response, after no response) # | 0.399 | |
| HR Time in response among responders# | 0.345 | |
| Response at landmark (3 months) # | 36% | 18% |
| Utility: Progression-free / Stable / In response* | 0.76 | 0.76 |
| Utility: Progressed / No response* | 0.70 | 0.70 |
| Drug costs (per cycle)* | £ 3,798 | £ 2,540 |
| Subsequent drug and administration costs (total)** | £ 1,000 | £ 4,500 |
| Administration costs (per cycle)* | £ 403 | £ 0 |
| Disease management costs - Progression-free / Stable / In response (per cycle)* | £ 92 | £ 92 |
| Disease management costs - Progressed (per cycle)* | £ 306 | £ 306 |
| Time to treatment discontinuation (median) # | 5.5 months | 1.5 months |

Sources: #hypothetical patient cohort; *NICE STA 2017: Nivolumab for treated or metastatic renal cell carcinoma (utilities from everolimus); **Assumption

# Base Case Results (Discounted)

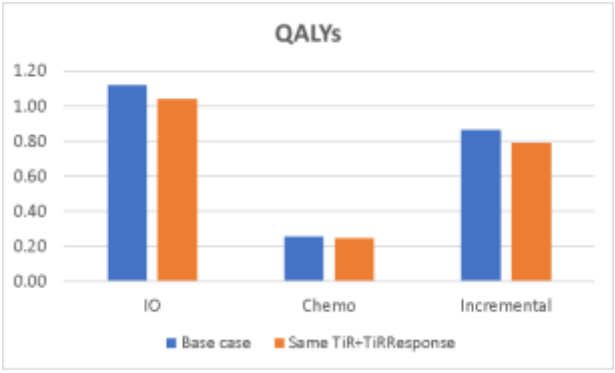
| | PartSA | | PartSA with landmark | | PatSA with response | |
|---|---|---|---|---|---|---|
| | IO | Chemo | IO | Chemo | IO | Chemo |
| **Total QALYs** | 1.12 | 0.26 | 1.74 | 0.39 | 1.12 | 0.26 |
| **Total costs** | £34,268 | £6,882 | £ 35,921 | £ 6,737 | £ 34,268 | £ 6,883 |
| **Drug acquisition costs** | £ 30,452 | £ 5,295 | £ 31,819 | £ 5,306 | £ 30,452 | £ 5,295 |
| **Drug administration costs** | £ 3,231 | £ 0 | £ 3,376 | £ 0 | £ 3,231 | £ 0 |
| **Monitoring costs** | £ 256 | £ 60 | £ 428 | £ 68 | £ 257 | £ 60 |
| **Disease management costs pre-progression / In response** | £ 83 | £ 19 | £ 119 | £ 37 | £ 83 | £ 19 |
| **Disease management costs post-progression / Not in response** | £ 174 | £ 41 | £ 309 | £ 31 | £ 174 | £ 41 |
| **Other costs** | £ 328 | £ 1,527 | £ 298 | £ 1,363 | £ 328 | £ 1,527 |
| **Incremental QALYs** | 0.86 | | 1.35 | | 0.86 | |
| **Incremental Costs** | £27,386 | | £29,184 | | £27,385 | |
| **ICER** | £ 31,756 | | £ 21,678 | | £ 31,902 | |

# Effect of Utilities/Costs

| | | Base case | | Response Scenario | | PFS Scenario | |
|---|---|---|---|---|---|---|---|
| ***Inputs*** | | **Utilities** | **Costs** | **Utilities** | **Costs** | **Utilities** | **Costs** |
| **Progression-free / Stable** | | 0.76 | £ 92 | 0.76 | £ 200 ↑ | 0.76 | £ 200 ↑ |
| **Stable** | | 0.76 | £ 92 | 0.72 ↓ | £ 225 ↑ | 0.72 ↓ | £ 225 ↑ |
| **Progressed** | | 0.70 | £ 306 | 0.70 | £ 250 ↓ | 0.40 ↓ | £ 1,000 ↑ |
| **In response** | | 0.76 | £ 92 | 0.80 ↑ | £ 50 ↓ | 0.76 | £ 200 ↑ |
| | | **QALYs** | **Costs** | **QALYs** | **Costs** | **QALYs** | **Costs** |
| ***PartSA*** | **Incremental** | 0.86 | £27,386 | 0.86 | £27,437 | 0.73 | £27,763 |
| | **ICER** | £ 31,756 | | £ 31,815 | | £ 37,924 | |
| ***PartSA with landmark*** | **Incremental** | 1.35 | £29,184 | 1.31 | £29,152 | 1.04 | £29,919 |
| | **ICER** | £ 21,678 | | £ 22,179 | | £ 28,732 | |
| ***PartSA with response*** | **Incremental** | 0.86 | £27,385 | 0.80 | £27,439 | 0.67 | £27,777 |
| | **ICER** | £ 31,902 | | £ 34,421 | | £ 41,656 | |

# Effect of Time in Response

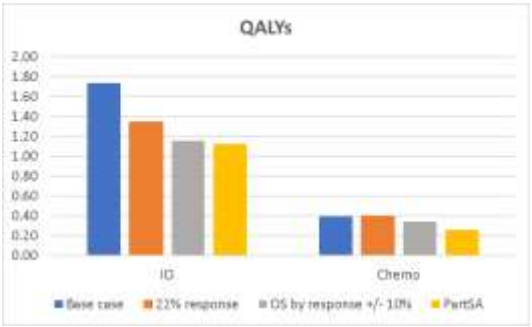
- Scenarios: Time in response for IO same as for Chemotherapy and Response based utility and costs scenario
  - E.g. utility in response 0.80 (base case 0.76)

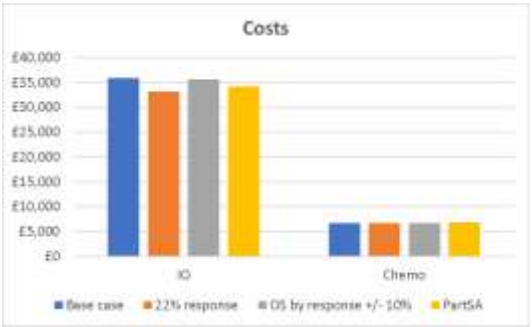



| PartSA with Response | Base case | New scenario |
|---|---|---|
| **Incremental QALYs** | 0.86 | 0.79 |
| **Incremental Costs** | £27,385 | £27,440 |
| **ICER** | £31,902 | £34,691 |

# Effect of Response Inputs

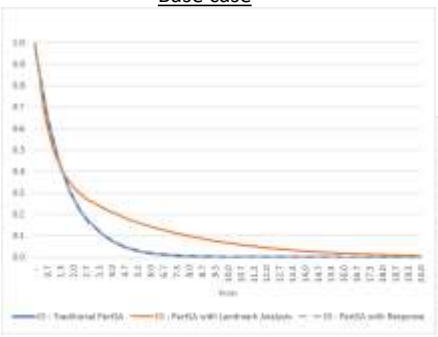
- Scenarios for PartSA with landmark analysis
  - Response rate 22% vs. 18% (base case: 36% vs. 18%)
  - OS by response +/-10% OS overall (base case: adjusted general mortality)



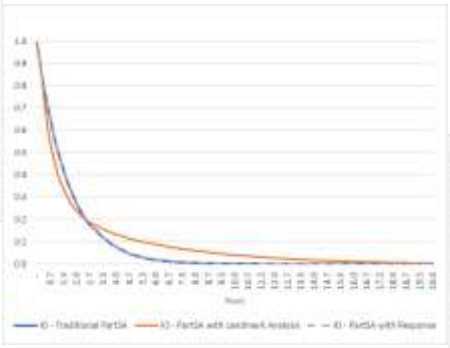



# Overall Survival with IO

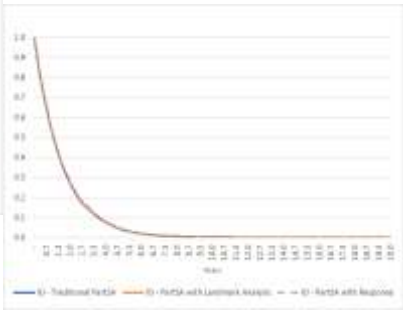
Base case



22% response for IO



OS by response +/-10%



# Conclusion

- The historically common approach might not be the most appropriate
- With the use of IOs in oncology, the role of response needs to be considered
- Base the modelling approach on careful assessment of the
  - Therapeutic area
  - Mechanism of action of comparators
  - Data
  - Uncertainties
- To incorporate the effect of response of treatment discontinuation and the change in response over time, time to event structure is recommended