Comparative Evaluation of the Performance of Two Value Attribution Frameworks for Combination Regimens in Oncology

Poster Number: HTA 230

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Background and Objective

- Traditional value assessment frameworks treat combination therapies in oncology as a single technology. Although the combination receives marketing authorisation, the company marketing the add-on submits the reimbursement dossier and is priced independently of the backbone therapy. Patient access to combinations therapies in oncology remains challenging for branded combinations with two or more sponsors given the difficulty of attributing appropriate proportional value to the individual components.
- Briggs[1] and Towse[2] have proposed two distinct value attribution frameworks to estimate the value attribution of individual component in a combination. We compared how these two frameworks perform in terms of recommended value split.

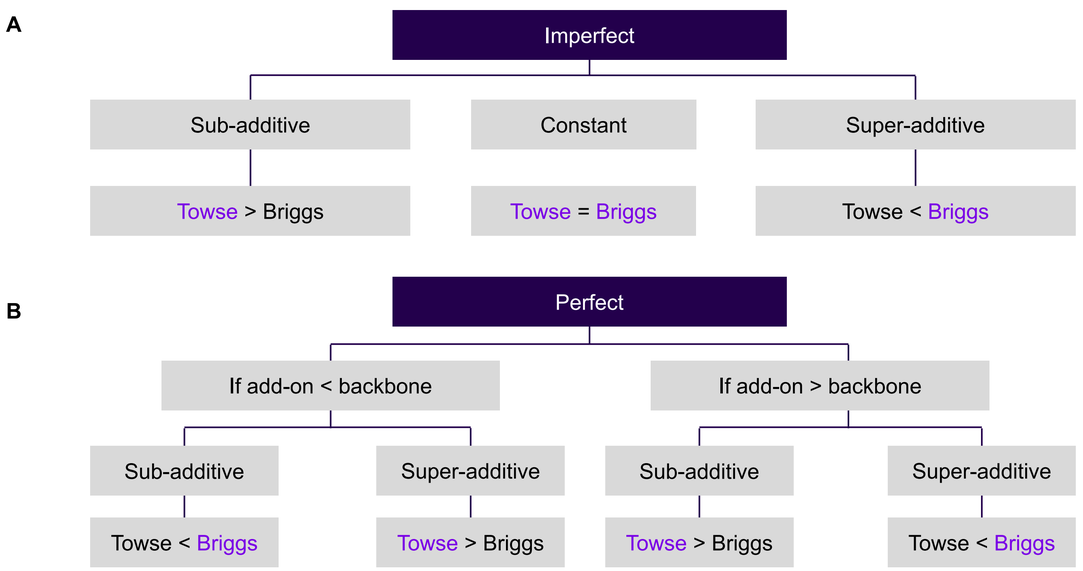
Methods

- An Excel-based model was developed to implement each framework and estimate the value split.
- The Excel model estimated value split based on quality adjusted life-year (QALY) and median PFS (mPFS) using the methodology outlined in both frameworks.
- Three hypothetical combinations were used to compare the result of these two frameworks in solving for the value attribution across combinations under different scenarios:
  - Case 1: Imperfect information, super additive, QALY (**Table 1**)
  - Case 2: Imperfect information, sub additive, mPFS (**Table 2**)
  - Case 3: Perfect information, mPFS, >2 components (**Table 3**)
- Simplifying assumptions were made, such as the assumption of balanced market power across components for Briggs; an equal value split for different components when applicable for Towse; value for add-on therapy based on assumptions for Towse in the imperfect information scenarios.

Results

- The results of value attribution for the same combination differed between these two frameworks because of the differences in the underlying assumptions and data requirements.
- With imperfect information and balanced market power, Briggs framework attributes more value to add-on therapies when the combination is assumed to be super-additive than the Towse approach. When the combination is assumed to be sub-additive, the add-on receives less value in the Briggs framework (**Figure 1A**).
- With perfect information, the Towse approach attributes more value to the add-on in super-additive combinations if its monotherapy value is worse than the backbone, whereas the add-on receives more value in the Briggs framework when the combination is sub-additive. Where the added value of the combination is constant additive, the value split is equal for both frameworks (**Figure 1B**).

Figures 1A and 1B: Comparison of the value attribution to the add-on therapy (vs. backbone) assigned by each framework by market scenario



Note: The coloured text indicates higher value attribution to the add-on therapy of the two frameworks.

Imperfect information	The independent benefit of one or more of the component therapies is unknown for the indication under consideration.
Perfect information	The independent benefit of all the component therapies is known for the indication under consideration.
Sub-additive	The **monotherapy benefit of each component** in the combination therapy **adds to more** than the combination therapy benefit. H(B) + H(A) > H(B+A) > max(H(A) H(B))
Constant additive	The **monotherapy benefit of each component** in the combination therapy is **equal to the sum** of the combination therapy benefit. H(B) + H(A) = H(B+A)
Super-additive	The **monotherapy benefit of each component** in the combination therapy **adds to less than** the combination therapy benefit. H(B) + H(A) < H(B+A)

Tables 1, 2 and 3: Model inputs and resulting value split across the three cases

Case 1: Imperfect information, super additive

Table 1 – Case 1 Model inputs	
Treatment	**mPFS (months)**
SoC	2.883
Treatment X (backbone)	4.088
Treatment X+Y (combo)	5.676

Table 1 – Case 1 Results		
Treatment	**Briggs**	**Towse**
Treatment Y (add-on) QALY	4.471[a]	3.486[b]
Value attribution X Inc. QALY (%)	1.205 (**43%**)	1.205 (**61%**)
Value attribution Y Inc. QALY (%)	1.588 (**57%**)	0.603 (**39%**)
Assumption	Constant Additive[a]	Super Additive

Inc.: Incremental (over SoC)

[a]When the health benefit value of add-on is unknown, the Briggs model implicitly assumes the benefit type of the combination is constant additive

[b]The value is based on the assumption that the incremental QALY (over SoC) of Treatment Y = 0.5 x incremental QALY of Treatment X: 3.486-2.883 = 0.5 x (4.088-2.883)

Case 2: Imperfect information, sub additive

Table 2 – Case 2 Model inputs	
Treatment	**mPFS (months)**
SoC	14.5
Treatment X (backbone)	27.6
Treatment X+Y (combo)	33.1

Table 2 – Case 2 Results		
Treatment	**Briggs**	**Towse**
Treatment Y (add-on) mPFS	20.0[a]	27.6[b]
Value attribution X Inc. mPFS (%)	13.1 (**70%**)	13.1 (**50%**)
Value attribution Y Inc. mPFS (%)	5.5 (**30%**)	13.1 (**50%**)
Assumption	Constant Additive[a]	Sub Additive

Inc.: Incremental (over SoC)

[a]When the health benefit value of add-on is unknown, the Briggs model implicitly assumes the benefit type of the combination is constant additive

[b]The value is based on the assumption that Treatment X mPFS = Treatment Y mPFS

Case 3: Perfect information

Table 3 – Case 3 Model inputs	
Treatment	**mPFS (months)**
Layer 1[a]	
SoC	4.9
Treatment X+Y (backbone)	8.4
Treatment Z (add-on)	5.4
Treatment X+Y+Z (combo)	12
Layer 2[a]	
SoC	0.5
Treatment X (backbone)	4.9
Treatment Y (add-on)	5.4
Treatment X+Y (combo)	8.4

Table 3 – Case 3 Results		
Treatment	**Briggs**	**Towse**
Layer 1[a]		-
Value attribution X+Y Inc. mPFS (%)	3.5 (**87%**)	-
Value attribution Z Inc. mPFS (%)	0.5 (**13%**)	-
Layer 2[a]		-
Value attribution X Inc. mPFS (%)	4.4 (**47%**)	-
Value attribution Y Inc. mPFS (%)	4.9 (**53%**)	-
Layer 1 & layer 2		-
Value attribution X Inc. mPFS (%)	(**41%** = 87% * 47%)	4.4 (**32%**)
Value attribution Y Inc. mPFS (%)	(**46%** = 87% * 53%)	4.9 (**34%**)
Value attribution Z Inc. mPFS (%)	(**13%**)	4.9 (**34%**)

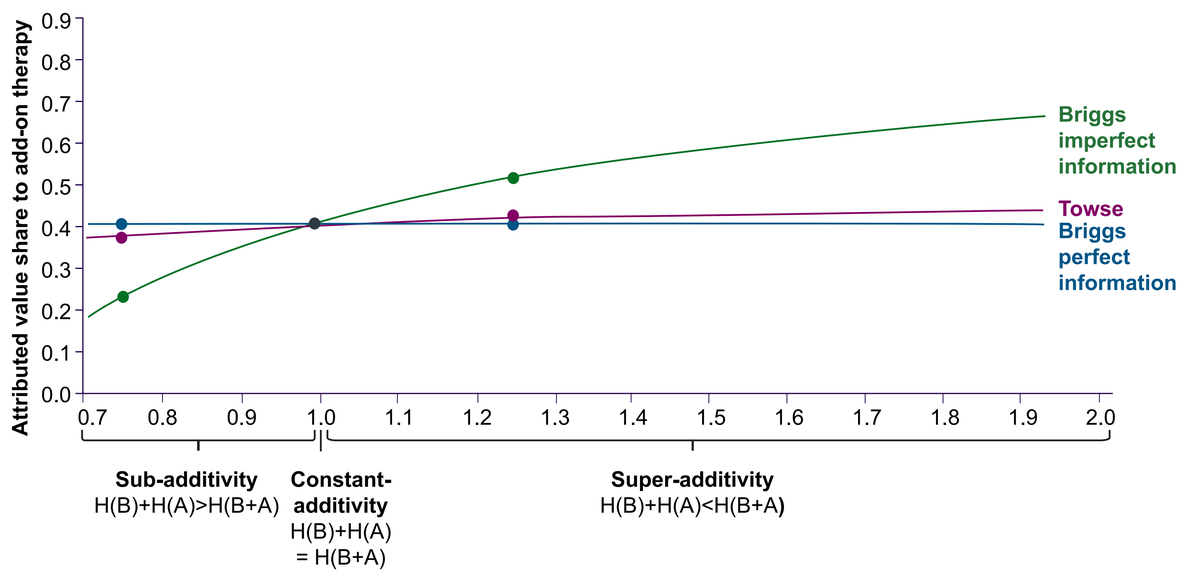
Inc.: Incremental (over SoC)

[a]Breakdown the combination therapy and determine the value split layer by layer

- 1st layer: solve for Z (add-on) and X+Y value split with X as the SoC
- 2nd layer: solve for Y and X value split, with best supportive care as SoC, and apply to prior Y+X combo value split

- The graph in **Figure 2** illustrates the difference in value split between Towse and the Briggs scenarios under different additivity assumptions.
- Briggs framework may overestimate/underestimate the value of add-on therapy if the combination is super-additive/sub-additive.
- This is shown by the green line being above the blue line in super-additivity region and the green line being below the blue line in the sub-additivity region.
- The Towse framework is closer aligned to Briggs perfect information indicating less bias in different additivity scenarios.
- This is shown by the purple line not diverging significantly from the blue line.

Figure 2: Graphical view of the difference in value split between Towse and the Briggs scenarios under different additivity assumptions



Conclusions

- **Both frameworks are valuable as they promote stakeholder dialogue and engagement on this topic. However, our findings demonstrate that they can lead to different conclusions depending on the available evidence. More research is needed before they are to be formally integrated in HTA and pricing negotiations.**
- **Both frameworks were deemed to have structural limitations that inhibit their implementation in clinical benefit-driven markets as they do not account for clinical plausibility, the non-linear relationship between price and incremental benefit, and do not capture the impact access to the combination may have on subsequent treatment eligibility and effectiveness.**

REFERENCES

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CONFLICTS OF INTEREST

YZ and MS: Sanofi —employees, may hold stock and/or stock options in the company.

JG, HS JJ and TC —employees of IQVIA, who were contracted to perform this research on behalf of Sanofi.

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