Clinical Trial Comparator Required for a Registration Trial

Assignment

- A biotechnology client determined that further investment in its non-TNF RA therapy could only be justified if the product would be used no later than 2nd line among non-TNF choices (3rd or 4th line overall assuming 1-2 lines of anti-TNF therapy). The assignment was a two-phase study to determine the attributes which would drive this prescribing preference and, most importantly, to assess the commercial value of a head-to-head trial

Key Tasks

- Develop a data and insight-based model of key prescribing drivers to support the therapy's forecast for the US and EU markets
- Determine the required target product profile necessary to achieve at least 2nd line use within non-TNF biologics
- Provide preference and market share estimates for a range of possible minimum and upside TPP scenarios, including the value of a head-to-head superiority trial, the benefits of demonstrating a pain and fatigue benefit and other key profile variations

Methodology

- In-depth qualitative interviews with KOLs followed by a web-based survey of >300 rheumatologists in the US, Germany and France

Deliverables

- 192 potential TPPs based on attribute and clinical trial design variations were reduced to nine scenarios that captured both the most essential variations and those that could be tested within the time constraints of a web survey
- Results provided a clear understanding of how attribute and clinical trial design variations would translate into market share and line of use, and also helped clarify the hurdles to achieving at least 2nd line use within non-TNF biologics

Preferred Sequence of Therapies

In the US, Therapy A or B is the preferred 1st line choice of 90% of physicians and 2nd line choice for 67% of physicians

Preferred Sequence of Therapies by Line of Treatment[1]
(percent of physicians)

	1st Line	2nd Line	3rd line	4th Line	5th Line	6th Line	7th Line
Therapy A	58%	23%	5%	1%	2%	3%	1%
Therapy B	31%	44%	9%	2%	1%	2%	2%
Therapy C	9%	18%	22%	10%	7%	4%	4%
Therapy D	0%	5%	36%	28%	10%	6%	3%
Therapy E	0%	1%	10%	18%	22%	17%	16%
Therapy F	1%	1%	6%	19%	30%	18%	8%
Therapy G	1%	5%	6%	10%	10%	17%	13%
Therapy H	1%	2%	5%	8%	11%	11%	14%
Clinical Trials	0%	1%	0%	1%	1%	5%	7%
Total[2]	100%	100%	100%	98%	94%	84%	69%

[1] *Colored bars represent lines where therapy is used predominantly. Anti-TNFs are marked in shades of blue*
[2] *Not all lines of therapy sum to 100% because not all physicians answered beyond three lines of therapy. Sum of columns may also differ from total due to rounding*

Question: What is your most common sequence of therapeutic choices for patients who are biologic treated. More specifically, which therapy do you typically use 1st, which do you use 2nd when your 1st choice fails?

Potentially Differentiating Attributes of Product X

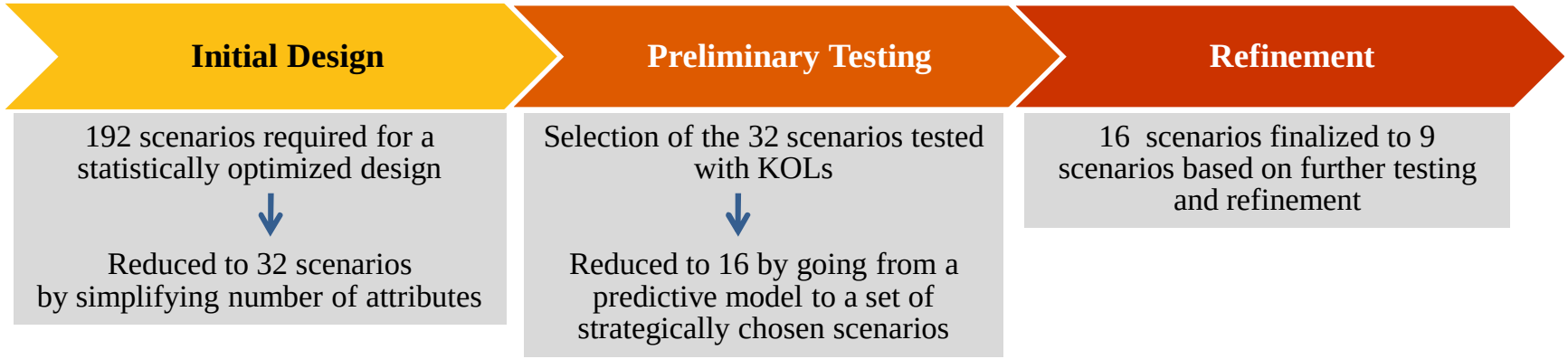
Attributes

Based on KOL feedback and insight from the Phase I study, the web survey was designed to predict how changes in four major attributes would translate into prescribing preferences

Attributes Varied in Analysis	Attributes Held Constant
Trial Design ▪ Superior to Humira in head-to-head (H2H) trial versus "no H2H trial"	**Inclusion criteria** ▪ Patients have failed MTX or failed MTX and at least one anti-TNF
Efficacy ▪ Comparable to efficacy of Humira or Actemra in historical placebo controlled trials	**Dosing** ▪ SC 2x/month
Safety ▪ Slightly safer than anti-TNFs (slightly lower rate of serious adverse events and no black box warning) versus anti-TNF-like safety	**Secondary Efficacy Endpoints** ▪ TSS, HAQ, HAQ-DI, QOL/SF-36
Pain and Fatigue ▪ Significant improvement in pain and fatigue over the drug against which it's being compared versus no improvement	**Time to Onset** ▪ Comparable to anti-TNFs
	Cost ▪ Price comparable to other biologic DMARDs

Design Process

The number of scenarios evaluated in the Web survey were eventually narrowed to nine based on internal analysis, testing with KOLs and reviews with the client



Scenarios Tested

Nine scenarios were tested. To simplify potential confusion in evaluating the relative value of one scenario compared to the next, the scenarios were presented in order of approximately least to most attractive

Product	Placebo Efficacy Similar To:	Head-to-Head Superiority Trial vs.:	Safety	Extra Improvement in Pain and Fatigue
A[1]	Humira	None	Anti-TNF like	No
B	Humira	None	Anti-TNF like	Yes
C	Actemra	None	Anti-TNF-like	No
D	Actemra	None	Anti-TNF-like	Yes
E	Actemra	Humira	Anti-TNF-like	No
F	Actemra	None	Slightly safer than anti-TNFs[2]	No
G	Actemra	None	Slightly safer than anti-TNFs[2]	Yes
H	Actemra	Humira	Slightly safer than anti-TNFs[2]	No
I	Actemra	Humira	Slightly safer than anti-TNFs[2]	Yes

[1] *Scenario A (the equivalent to Humira) was included as a dummy scenario for the purpose of validating responses*

[2] *Described as a rate of serious adverse events slightly less than anti-TNF and no black box warning*