DANCING WITH THE DRAGON: CONSIDERATIONS AND LEARNINGS IN THE 2019 CHINA NRDL NEGOTIATIONS

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INTRODUCTION

The NRDL has become an important cornerstone of patient access to innovative treatments in China since the regular annual updates began in 2017; therefore, understanding the strategies that manufacturers employ and necessary considerations associated with the NRDL inclusion have become increasingly important. Taking a closer look at the negotiation tactics used for specific drug classes and therapeutic area characteristics provides stakeholders with a greater opportunity to understand which negotiation tactics may be applied to novel products. In turn, this can facilitate more successful NRDL negotiation outcomes and timely patient access to innovative treatments.

OBJECTIVES

Our research aimed to evaluate the outcomes of the 2019 NRDL negotiations involving PD-1 / PD-L1 (PDx) inhibitors and direct-acting anti-viral agents (DAA) products and share key learnings with stakeholders.

METHODOLOGY

Secondary research was conducted to identify the 2019 NRDL listing status of PDx and DAA products and to understand the competitive landscape and dynamics in the oncology and hepatitis C disease space, that may have impacted the negotiation outcomes.

RESULTS

The outcomes of the 2019 NRDL negotiations are summarized in Figure 1.

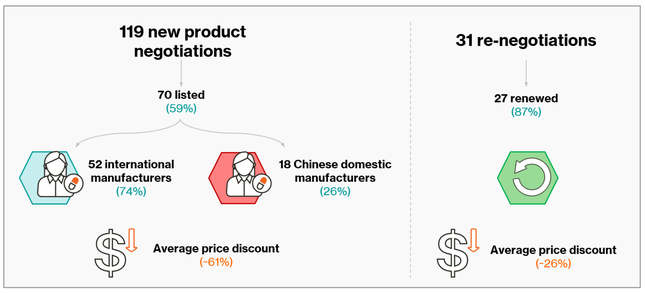

FIGURE 1: 2019 NRDL NEGOTIATION OUTCOMES & AVERAGE PRICE DISCOUNT

Negotiation Tactic	Approach
Comparative Negotiation	• Pre-negotiation assessment is completed by a committee of pharmacoeconomic experts to assess funding feasibility • 'Base price' is established for use during the negotiations (note: this is not disclosed to the manufacturer) • The final agreed price must not exceed this 'base price', and manufacturers have 2 opportunities to offer a suitable price • If both prices exceed the base price by 15%, the product cannot be included on the NRDL update
Competitive Negotiation	• No 'base price' is established • Manufacturers provide their best price offers and the lowest-priced offer enters the NRDL with 2 years of exclusivity

FIGURE 2: COMPARATIVE & COMPETITIVE NEGOTIATION APPROACH

The negotiation tactics employed by the National Healthcare Security Administration (NHSA) during the 2019 NRDL negotiations can be characterized as either comparative negotiation, which was used in most therapeutic areas, or competitive negotiation, which was used during negotiations involving the DAA products in the hepatitis C therapeutic area. Figure 2 outlines how the comparative and competitive negotiation tactics were employed in practice during the negotiations.

PDx NRDL DYNAMICS

	International Manufacturer			Chinese Domestic Manufacturer			
Brand Name	**KEYTRUDA**	**OPDIVO**	**IMFINZI**	**TREIPRIL**	**TYVYT**	**AIRUIKA**	**BAIZEAN**
Molecule Name	Pembrolizumab	Nivolumab	Durvalumab	Toripalimab	Sintilimab	Camrelizumab	Tislelizumab
Mechanism of Action	PD-1	PD-1	PD-L1	PD-L1	PD-1	PD-1	PD-1
Manufacturer Name	MERCK	BMS	ASTRAZENECA	JUNSHI BIOSCIENCES	INNOVENT	HENGRUI MEDICINE	BEIGENE
First Regulatory Approval Date	JULY 2018	JUNE 2018	DECEMBER 2019	DECEMBER 2018	DECEMBER 2018	MAY 2019	DECEMBER 2019
Regulatory Approved Indications	2L melanoma 2L esophageal cancer 1L non-squamous non-small cell lung cancer 1L PD-L1 positive non-small cell lung cancer	3L gastric cancer 2L PD-L1 positive non-small cell lung cancer 2L head & neck squamous cell carcinoma	Unresectable stage III non-small cell lung cancer	2L melanoma	3L+ RR & classic Hodgkin lymphoma	3L+ RR & classic Hodgkin lymphoma 2L+ advanced hepatocellular carcinoma 2L esophageal squamous-cell carcinoma 1L non-squamous non-small cell lung cancer	3L+ RR & classic Hodgkin lymphoma 2L PD-L1 urothelial cancer 2L PD-L1 urothelial cancer
2019 NRDL Inclusion	NO	NO	NOT ELIGIBLE	NO	YES	NOT ELIGIBLE	

FIGURE 3: PDx PRODUCT NRDL ELIGIBILITY, INDICATIONS & OUTCOMES

Due to the high unmet need for new treatment options, the PDx NRDL inclusion had been long awaited in China, with a total of four PDx products eligible for the 2019 NRDL negotiations (pembrolizumab, nivolumab, toripalimab, and sintilimab). Several other PDx products (durvalumab, camrelizumab, tislelizumab) were unable to participate in the 2019 NRDL negotiations as the regulatory approval dates did not meet the December 2018 cut-off as summarized in Figure 3.

Only sintilimab was successfully included on the 2019 NRDL, likely due to the willingness to provide a steeper discount vs. other PDx manufacturers, as well as the small budget impact associated with its classic Hodgkin lymphoma target population compared to the other larger PDx approved indications (i.e., non-small cell lung cancer and head and neck squamous cell carcinoma).

Background considerations on the competitive environment and the trade-off between discounting and sales volume provide further context around the negotiation outcomes:

COMPETITION:

INNOVENT was likely aware of the impending launch of HENGRUI's camrelizumab and BEIGENE's tislelizumab, which both received NMPA marketing authorization in the same indication as sintilimab after the 2019 NRDL eligibility cut-off date

HENGRUI MEDICINE and BEIGENE are known to have strong marketing teams in China, which likely motivated INNOVENT to discount during the 2019 NRDL negotiations to grow its market share ahead of competitors achieving reimbursement

DISCOUNT IN EXCHANGE FOR VOLUME:

To secure a spot on the NRDL, sintilimab underwent a 64% price cut, resulting in an annual price reduction from CNY 217,717 (~ USD 32,700) to CNY 98,557 (~ USD 14,800)

The Q1 2020 sales for sintilimab were reported as CNY 0.4 billion despite the hospital visit interruption due to the COVID-19 pandemic, and assuming the sales growth continues at this rate throughout 2020, the resulting annual sales of CNY 1.6 billion would mean that the discount / volume trade-off was worthwhile as shown in Figure 4

Going forwards, sintilimab's price point will become the benchmark for future PDx NRDL negotiations. In April 2020, sintilimab was approved by the NMPA for the treatment of 2L PD-1 positive locally advanced or metastatic urothelial cancer, and the NMPA has also recently accepted a supplemental new drug application for sintilimab for 1L advanced or metastatic squamous NSCLC, putting it in direct competition with pembrolizumab. These dynamics, and the entry of additional PDx products (e.g., ROCHE's atezolizumab) will further accelerate the downward pricing pressure. In therapeutic areas with strong competition (as was seen in the PDx space), the NHSA tends to test the water by first reimbursing one product in a small indication to understand the real-world budget impact and funding sustainability. This will also set the price benchmark for future entrants.

HEPATITIS C NRDL DYNAMICS

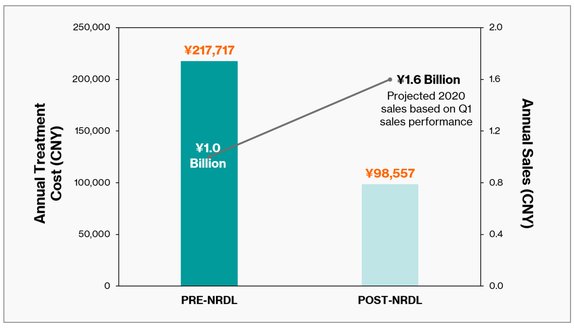

FIGURE 4: COMPARISON OF SINTILIMAB PRE & POST NRDL PRICE AND VOLUME

The NHSA leveraged a competitive negotiation in the hepatitis C disease space, involving four companies, three international (MERCK, GILEAD, and ABBVIE) and one Chinese domestic manufacturer (ASCLETIS PHARMA) as summarized in Figure 5. The bidding-like negotiation involved manufacturers competing for steep discounts in exchange for two-year exclusivity on the NRDL and was selected since the DAA products are largely seen to be clinically undifferentiated from an efficacy perspective.

The winners in the hepatitis C space included international manufacturers only, with MERCK'S elbasvir / grazoprevir and GILEAD's ledipasvir / sofosbuvir and sofosbuvir / velpatasvir managing to secure a spot on the NRDL after negotiating the lowest full-course cost, translating to an average price cut of ~86%. Danoprevir's failure to secure a spot on the NRDL led to a stock price plunge for ASCLETIS PHARMA by 25%, signifying the importance of NRDL inclusion given the curative nature of DAAs.

	International MFGs					Chinese Domestic MFGs
Brand Name	**ZEPATIER**	**HARVONI**	**EPCLUSA**	**EXVIERA**	**VIEKIRAX**	**GANOVO**
Molecule Name	elbasvir / grazoprevir	ledipasvir / sofosbuvir	sofosbuvir / velpatasvir	dasabuvir	ombitasvir / paritaprevir / ritonavir	danoprevir
Manufacturer Name	MERCK	GILEAD		ABBVIE		ASCLETIS PHARMA
Regulatory Approved Indication	Hepatitis C Genotype 1a, 1b, 4	Hepatitis C Genotype 1, 4, 5, 6	Hepatitis C Genotypes 1-6	Hepatitis C Genotype 1a, 1b	Hepatitis C Genotype 1a, 1b, 4	Hepatitis C Genotype 1b
First Regulatory Approval Date	APRIL 2018	NOVEMBER 2018	MAY 2018	MAY 2018	SEPTEMBER 2017	JUNE 2018
2019 NRDL Inclusion	YES	YES	YES	NO	NO	NO

FIGURE 5: HEPATITIS C PRODUCT NRDL OUTCOMES

CONCLUSION

Competitive landscape dynamics are often transferable between therapeutic areas and drug classes; therefore, mapping these landscape dynamics enables a better understanding of which negotiation tactics the NRDL committee could employ. This will enable manufacturers to better prepare for negotiation scenarios and improve the probability of successful NRDL inclusion, facilitating patient access.

RECOMMENDATIONS

Manufacturers of products competing in the same space as products that have been included on the NRDL should closely examine current pricing dynamics. The established NRDL price will be considered as the benchmark during new negotiations. In this scenario, manufacturers should consider leveraging an indirect treatment comparison vs. competitor products to support the differential value proposition and pricing opportunity.

The 2019 NRDL negotiations employed new approaches in unique disease areas. In order to be successful, manufacturers will need to understand the negotiation rules, as well as the current and future competitive landscapes, to support timely patient access to innovative treatments in China.