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Surrogate Survival Endpoints: Are They Sufficient to Support Access?

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Richard Macaulay Vice President, Global Pricing & Market Access, PRECISIONadvisors

Richard is responsible for the growth and development of consultative, analytic, and data services supporting life science products' commercial performance. Our team excels at understanding the ever-changing and complex healthcare market and helping clients solve issues including access strategy, stakeholder mapping, value communication, strategic pricing, and product positioning.

Surrogate Survival Endpoints: Are they Sufficient to Support Access?

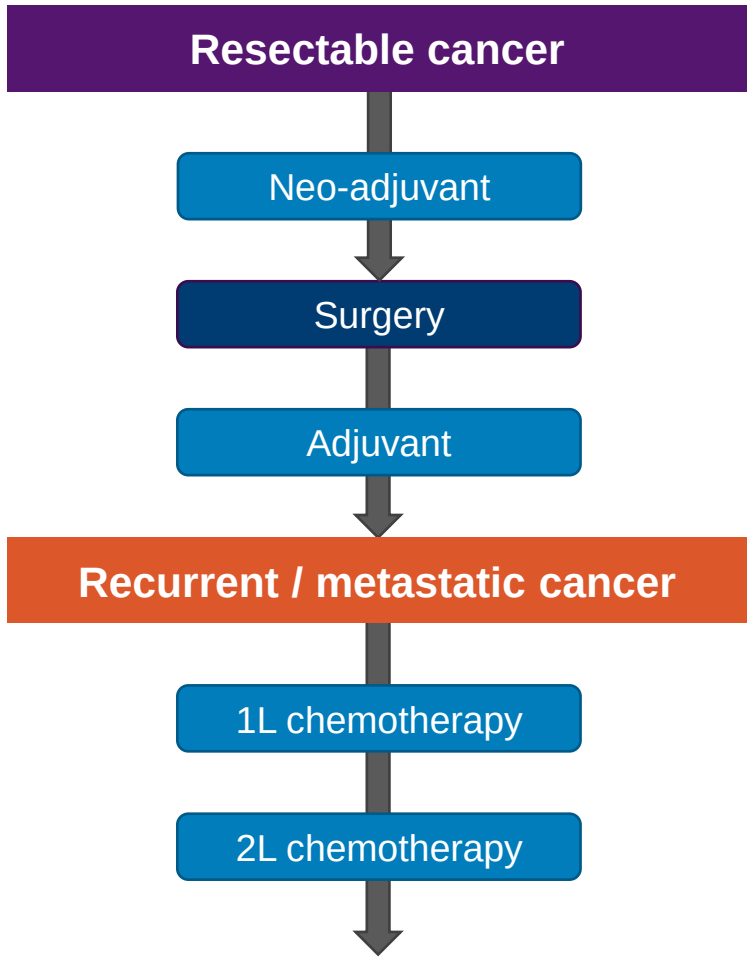
Agenda

1	Evolving oncology landscape
2	Payer challenges
3	HTA outcomes
4	Conclusions

Oncology drugs are being increasingly developed as earlier-line therapies

Evolving oncology treatment landscape

Typical treatment pathway



Traditional focus

for cancer drug development

*The risk/benefit of traditional chemotherapies limits their use to the **palliative** setting*

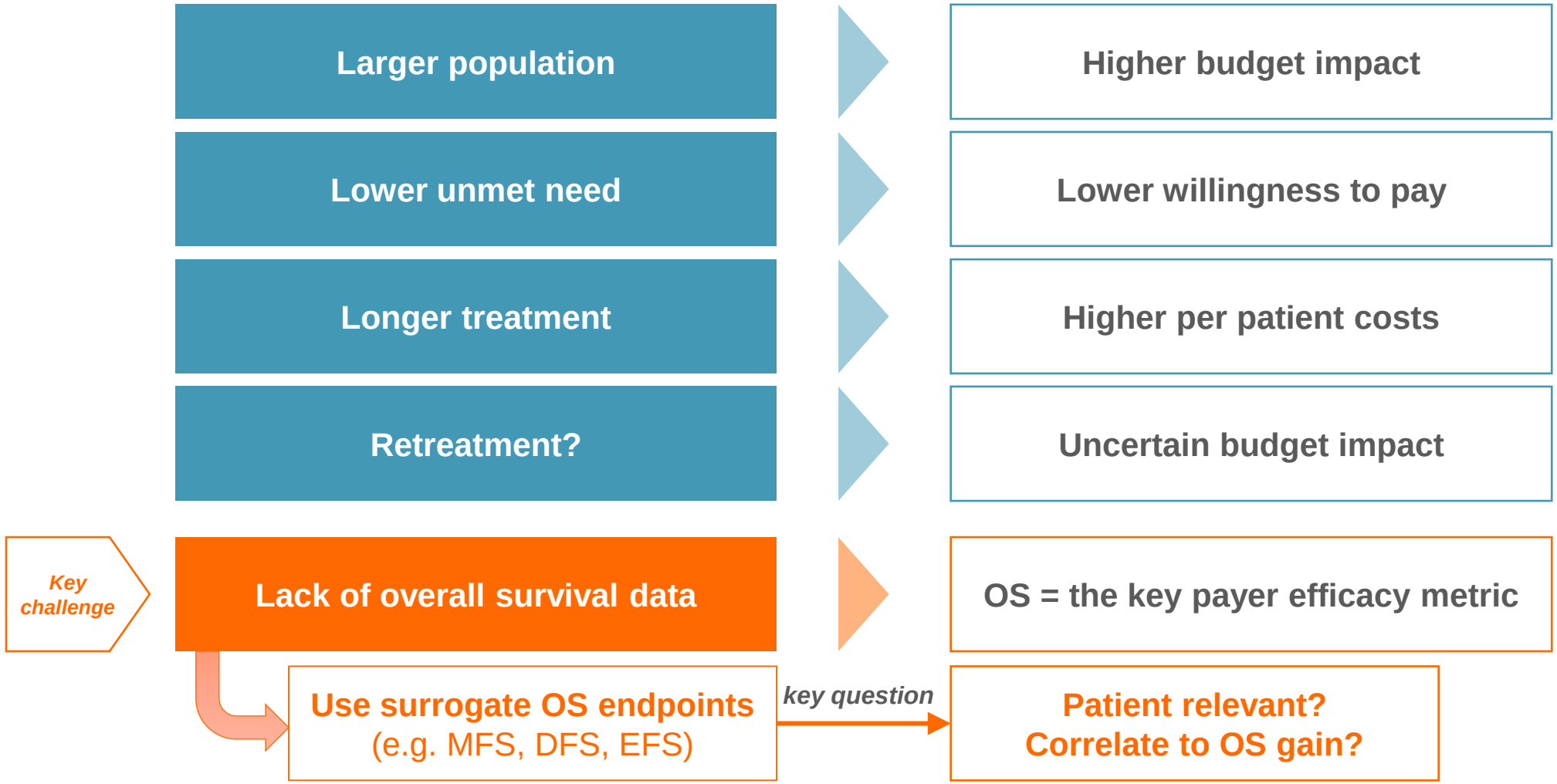
New focus

for cancer drug development

*Newer therapies (e.g. I-Os) with **long-term OS** benefits & favorable **safety** can justify **earlier use***

Developing oncology drugs for early-stage use can create challenges for payers

Payer challenges for oncology therapies in the neo-/adjuvant setting (vs. the metastatic setting)



This research examined how early-stage oncology drugs were assessed by payers

Research objectives & methodology

Identify any EC-approved therapy for **neo-/adjuvant cancer**

(1st Jan 2011 to 30th May 2021)

Corresponding HTA guidance identified for


HAS


NICE


SMC


G-BA


CADTH


PBAC


Medicinrådet

Key information extracted with a focus on **surrogate OS endpoint critique**

9 drug:indication pairings were identified with neo-/adjuvant oncology indications

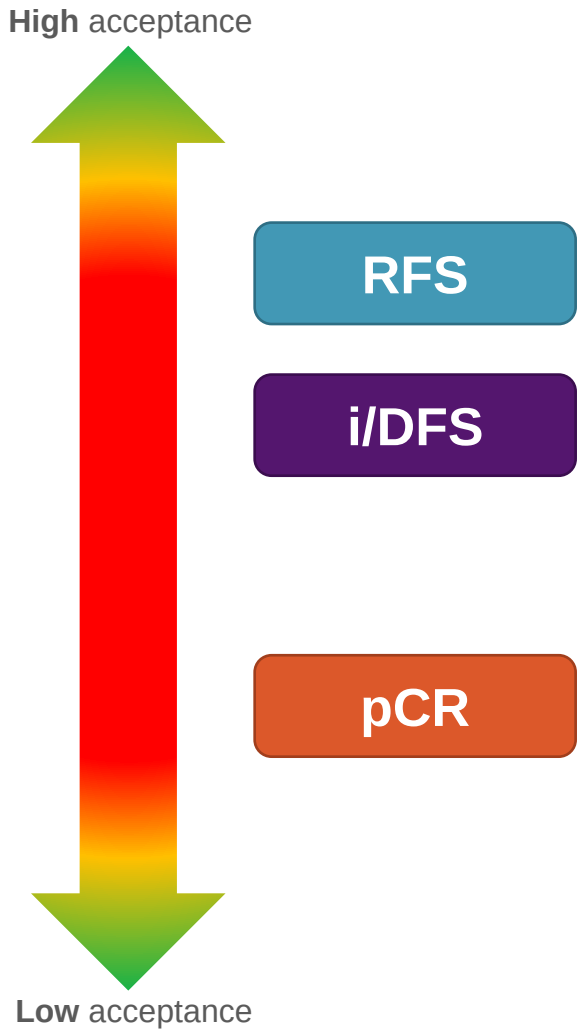
Brand name	INN	Indication			EC-approval date	Primary endpoint
		Stage	Biomarker	Cancer		
HERCEPTIN	Trastuzumab	Post-Adj	HER2+	Breast	Jun 2006	**DFS**
HERCEPTIN	Trastuzumab	Adj	HER2+	Breast	Mar 2011	**DFS**
PERJETA	Pertuzumab	Neo	HER2+	Breast	Jul 2015	**pCR**
PERJETA	Pertuzumab	Adj	HER2+	Breast	Jun 2018	**iDFS**
NERLYNX	Neratinib	Adj	HER2+	Breast	Jun 2018	**iDFS**
OPDIVO	Nivolumab	Adj	-	Mel	Jul 2018	**RFS**
TAFINLAR + MEKINIST	Dabrafenib + trametinib	III	BRAF+	Mel	Aug 2018	**RFS**
KEYTRUDA	Pembrolizumab	III	-	Mel	Dec 2018	**RFS**
KADCYLA	Trastuzumab emtansine	Adj	HER2+	Breast	Dec 2019	**iDFS**

51 HTA outcomes of early-stage oncology therapies were identified

Brand name	Indication			Primary endpoint	HTA appraisal						
	Stage	Biomarker	Cancer								
HERCEPTIN	Post-Adj	HER2+	Breast	**DFS**			ASMR I				
HERCEPTIN	Adj	HER2+	Breast	**DFS**			ASMR II				
PERJETA	Neo	HER2+	Breast	**pCR**			SMR insuff	No benefit			
PERJETA	Adj	HER2+	Breast	**iDFS**			SMR insuff	Minor			
NERLYNX	Adj	HER2+	Breast	**iDFS**			SMR insuff	Minor			
OPDIVO	Adj	-	Mel	**RFS**			ASMR III	Non-quant.			
TAFINLAR + MEKINIST	III	BRAF+	Mel	**RFS**			ASMR III	Considerable			
KEYTRUDA	III	-	Mel	**RFS**	CDF		ASMR III	Non-quant.			
KADCYLA	Adj	HER2+	Breast	**iDFS**			ASMR III	Major			

HTA outcome key	Positive	Moderate/conditional	Negative	Not assessed

Acceptability of early-stage oncology therapies varied by **surrogate endpoint**



- Payer assessments were most positive where:
  - the **magnitude** of the surrogate benefit were **greater**
  - **early OS** data showed significant benefits or a clear numerical trend
- Nevertheless, there were some **trends** regarding acceptability of **endpoints across payers**
  - Although clearly valued **less than OS**, RFS and DFS were deemed patient relevant by payers, much **moreso than pCR**

Acceptability of early-stage oncology therapies varied by **HTA body**

- NICE and SMC appeared the most supportive of **access for oncology drugs using surrogate endpoints**, followed G-BA, with CADTH the least
- Some assessments (e.g. NICE & G-BA) were **conditional** and contingent on more **mature follow-up data** being provided for reassessment
- PBAC imposed flow-on restrictions **limiting retreatment** with I-Os in later lines of therapy

Early-stage cancer therapies supported by surrogate survival endpoints have achieved some payer access, with variations between different endpoints & payers

Summary and conclusion

Oncology therapies approved and reimbursed in metastatic cancer are being **increasingly investigated in the early-stage setting** using **surrogate survival metrics** as primary endpoints

HTA bodies have generally given **quite favorable assessments** to these early cancer therapies, deeming some surrogate endpoints **patient relevant or correlated to OS**

There are, nevertheless, clear **trends in payer willingness to accept** these endpoints **between** different **surrogate endpoints** and between different **HTA bodies**

Further, such therapies may be **more likely to be subject to reimbursement conditional on further evidence** generation [e.g. CDF] and/or later-line restrictions

THANK YOU!

we look forward to staying in touch

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