Managed access agreements (MAAs) and continuing data collection after provisional positive recommendation from the National Institute for Health and Care Excellence (NICE)

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Introduction

A managed access agreement (MAA) is a temporary arrangement between NICE and a manufacturer, which allows patients to gain access to new treatments while more safety and efficacy data are collected, allowing NICE to make a final recommendation.

The Cancer Drugs Fund (CDF) was re-established as a managed access scheme in February 2016, while in April 2013, the Highly Specialised Technology programme (HSTP) replaced the Advisory Group for National Specialised Services (AGNSS) for the assessment of ultra orphan drugs.

Both new programmes include the possibility of MAAs to resolve any significant clinical uncertainty after consideration by NICE. At the time of writing, NICE have not implemented any MAAs outside the CDF or HSTP. Therefore, all MAAs discussed are part of the CDF or HSTP. All treatments within the CDF have MAAs.

Objectives

The aim of this research was to conduct a comprehensive review of all UK Health Technology Assessments (HTAs) with MAAs up to 31st August 2018, comparing them within and between the CDF and HSTP.

Methods

All NICE submissions with published MAAs up to 31st August 2018 were identified from the NICE database for the CDF and HSTP. Data were extracted for evidence source and type. The SIRIUS Oncology HTA Database† was used to make comparisons with NICE technology appraisals without MAAs. The SIRIUS Oncology HTA Database contains details of all NICE assessments since December 2010, with corresponding data for SMC, HAS, G-BA/ IQWiG, PBAC, and pCODR assessments for the included treatments and indications.

Results

- Within the CDF, 14 treatments had MAAs for 18 separate indications. Fifteen of the 18 MAAs continued data collection from the ongoing key clinical trials (phase II-III) until they reached data maturity/trial completion, 13 specifying this as the primary source (**Table 1**). The MAAs for TA446 and TA447 have been concluded, and both treatments were subsequently recommended by NICE.
- All 18 MAAs within the CDF also collected retrospective data from the (mandated) Systemic Anti-Cancer Therapy (SACT) dataset, and 14 utilised the Blueteq database, owned by Public Health England and NHS England, respectively. Four MAAs utilised SACT as the primary data source (**Table 1**).

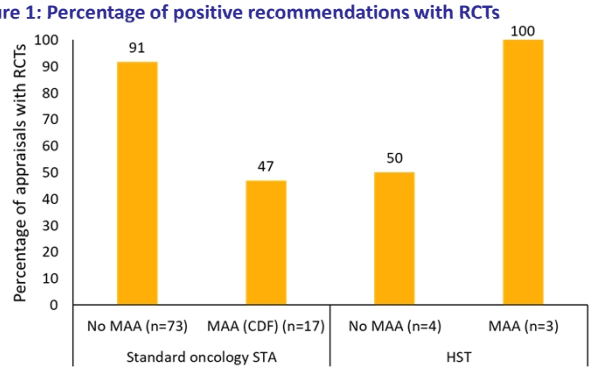
Table 1: Source of data during the MAA for CDF

Treatment	NICE reference	Clinical trial			Blueteq	SACT	End date	Length (months)
		Included	Primary	Phase	Included	Primary		
Atezolizumab	TA492	Y	Y	III	Y	N	Dec 2020	38*
Avelumab	TA517	Y	Y	II	Y	N	Feb 2020	11*
Brentuximab	TA446	N	-	-	Y	N	Nov 2017	5
Crizotinib	TA529	Y	N	II	Y	Y**	Apr 2023	5 years
Daratumumab	TA510	N	-	-	Y	Y**	Nov 2020	3 years
Ibrutinib	TA491	Y	N	II & III	Y	Y	Sept 2020	3 years
Ixazomib	TA505	Y	Y	III	Y	N	Dec 2019	27*
Venetoclax	TA487	N	-	-	N	Y	Dec 2020	38*
Pembrolizumab	TA519	Y	Y	III	Y	N	Dec 2018	7*
Pembrolizumab	TA447	Y	Y	III	N	N	Dec 2017	6*
Pembrolizumab	TA522	Y	Y	III	Y	N	Nov 2019	15*
Osimertinib	TA416	Y	Y	II	N	N	Mar 2019	30
Niraparib	TA528	Y	Y	III	Y	N	Jun 2020	22*
Nivolumab	TA483	Y	Y	III	Y	N	Jun 2019	20*
Nivolumab	TA484	Y	Y	III	Y	N	Jun 2019	20*
Nivolumab	TA490	Y	Y	III	Y	N	Sept 2019	21*
Obinutuzumab	TA472	Y	Y	III	Y	N	Dec 2020	39*
Olaratumab	TA465	Y	Y	III	N	N	Dec 2020	41*

Y, yes; N, no; NICE, National Institute for Health and Care Excellence; SACT, Systemic Anti-Cancer Therapy. *Calculated from date of issue for MAA and end of MAA. **Primary source was SACT and other Public Health England datasets.

- Three treatments were identified in the HSTP that were provisionally recommended with MAAs: ataluren, asfotase alfa, and elosulfase alfa. Within the MAAs, data collection is ongoing for all UK patients. For the latter two treatments, specific databases were set up, while for ataluren, ongoing storage utilises the NorthStar database for Duchenne Muscular Dystrophy.
- The HSTP has a strict 5 year MAA, whereas the CDF is usually (but not exclusively) limited to 2 years, often ending at the completion of the clinical trial.
- All MAAs within the HSTP specify an exit strategy that includes the cessation of funding for all patients, including those on treatment, if NICE reaches a negative opinion. Whereas, guidance for CDF MAAs states that, under these conditions, patients on treatment can continue at the expense of the manufacturer.
- The percentage of oncology treatments recommended within the CDF (i.e. with MAAs) that had RCTs was 47%, compared with 91% for treatments recommended outside the CDF (i.e. without MAAs), indicating oncology treatments without RCTs were more likely to require MAAs (**Figure 1**). However, HSTP treatments recommended with MAAs were approximately twice as likely to have RCTs as those without MAAs (**Figure 1**).

Figure 1: Percentage of positive recommendations with RCTs



HST, Highly Specialised Technology; MAA, managed access agreement; RCT, randomised controlled trial; TA, technology appraisal. For CDF, n=17 (not 18) as pre-MAA trial data for TA447 are no longer available, updated to TA531, once MAA was completed.

Conclusions

As of August 2018, there are 18 HTAs within the CDF, and three within the HSTP that have MAAs. Most MAAs for the CDF had multiple data sources, including the SACT (18 of 18) and Blueteq databases (14 of 18), often with phase II-III clinical trials as the primary data source (13 of 18). The HSTP MAAs collect real-world data for all patients treated in the UK over a strict 5-year period, while the CDF MAA is often around two years, but can also link to the completion of the clinical trial. The percentage of oncology treatments recommended within the CDF that had RCTs was around half those recommended without MAAs, but the opposite pattern was observed in HSTs.

References
1. https://www.nice.org.uk/guidance
2. https://www.scottishmedicines.org.uk/medicines-advice

† Ask a member of the SIRIUS team for more information.