Horizon Scanning

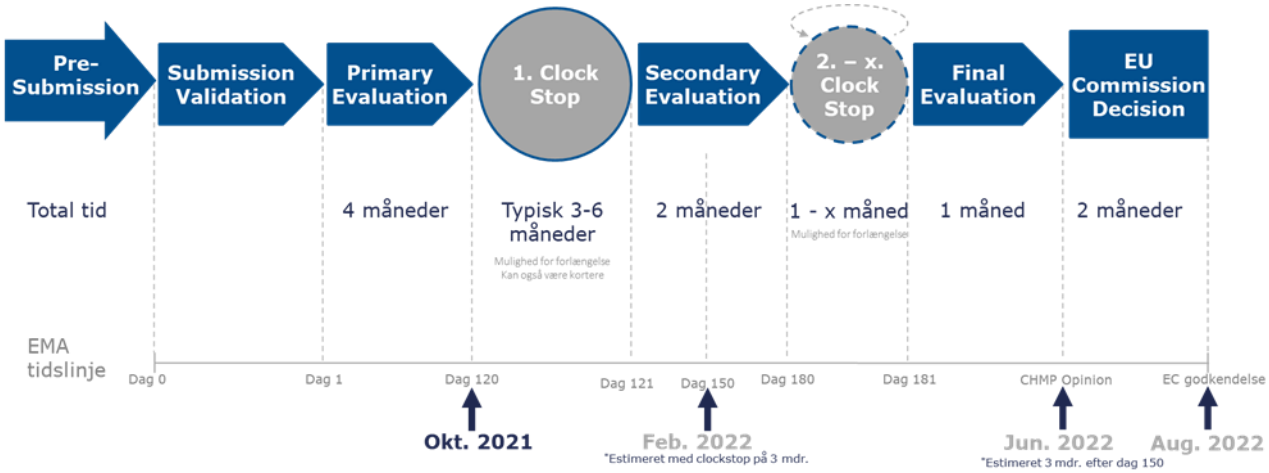
Orientering om nyt lægemiddel: Mobocertinib

Lægemiddelstof:	Mobocertinib
Produkt navn:	(EXKIVITY)
ATC-kode:	L01X-E
Dispenseringsform:	Oralt[1]
Anvendelsesområde:	Treatment of adult patients with epidermal growth factor receptor (EGFR) exon 20 insertion mutation-positive locally advanced or metastatic non-small cell lung cancer (NSCLC)[2]
Virksomhed:	Takeda
Sektor:	Formodentlig sekundær sektor

Udarbejdet: 5. oktober 2021

Status for godkendelse[2]

Estimeret tidsperspektiv for markedsføringstilladelse i Danmark:
(Godkendes via proces for nye lægemidler, som orphan. Procedurenummer EMEA/H/C/005621)



Beskrivelse af nyt lægemiddel[1,3,4]

The succinate salt form of mobocertinib, an orally available inhibitor of human epidermal growth factor receptor (EGFR) exon 20 insertion mutations, with antineoplastic activity. Upon oral administration, mobocertinib, and its active metabolites, specifically and irreversibly binds to and inhibits exon 20 insertion mutations of EGFR. This prevents EGFR-mediated signaling and leads to cell death in tumor cells expressing exon 20 insertion mutations. In addition, mobocertinib may inhibit the activity of other EGFR family members, such as human epidermal growth factor receptor 2 (HER2; ERBB2) and HER4. EGFR, HER-2 and -4 are receptor tyrosine kinases often mutated in numerous tumor cell types. They play key roles in tumor cell proliferation and tumor vascularization.

First-in-class tyrosine kinase inhibitor of activating exon 20 mutations in EGFR and HER2

Exkivity (mobocertinib) er godkendt af FDA:
https://www.accessdata.fda.gov/mobocertinib

Sygdomsbeskrivelse og patientgrundlag[5,6]

Definition, lungekræft:

- Alle kræftformer i lunger og bronkier
- Ca. 90 % af alle tilfælde af lungekræft opstår i bronkierne
- På grund af behandlingen skelnes der mellem småcellet og ikke-småcellet karcinom (pladeepitel karcinom, adenokarcinom og storcellet karcinom)
- Småcellet lungekræft er den mest aggressive form for lungekræft, som vokser hurtigt og spreder sig tidligt

Omtrent 4.600 danskere diagnosticeres årligt med lungekræft. Heraf har ca. 140 en aktiverende Epidermal Growth Factor Receptor (EGFR) mutation. Flertallet af disse patienter får progression, og metastaser i centralnervesystemet (CNS) optræder hyppigt.

Epidermal growth factor receptor (EGFR) is one of several unique, genetic alternations found in NSCLC that affects approximately 15-21% of all NSCLC patients. Approximately 1%-2% of NSCLCs have an in-frame insertion in exon 20 of EGFR resulting in innate resistance to 1st generation TKIs. Takeda estimates that there are approximately 30,000 patients diagnosed with EGFR Exon20 insertion mutation-positive NSCLC worldwide each year.

Standardbehandling/ andre behandlingsmuligheder til indikationen[6,7]

Medicinrådet har udarbejdet anbefalinger på lægemidler og indikationsudvidelser på en række lægemidler til behandling af lungekræft:
https://medicinraadet.dk/om-os/fagudvalg/lungekraeft

Generelt om behandlingen

- Kun knap 25 % af patienterne er operable og en del af disse viser sig under operationen også at være inoperable
- Patienter med ikke-småcellet lungekarcinom bør testes for genmutationer (især EGFR og ALK) og ekspressionsgrad af overflademarkører (programmeret celledød ligand 1 PD-L1)), da dette har indflydelse på, om patienten skal have hhv. targeteret- eller immun-terapi

Status for dokumentation[8]

Studier:

Land, Population, Studienr.	Intervention	Komparator	Primær outcome	Sekundær outcome	Afsluttet
Flere lande, Fase II, N = 395, NCT02716116[a]	Drug: TAK-788 TAK-788 capsules. Other Name: AP32788 Drug: TAK-788		Part 1, Dose Escalation Component: RP2D of Orally	Parts 1, 1A, 1B and 2, Dose Escalation and Expansion Cohorts: Safety Analysis of TAK-788 and when TAK-788	March 2023

	TAK-788 capsules. Other Name: AP32788 Drug: Pemetrexed Pemetrexed intravenous infusion. Drug: Carboplatin Carboplatin intravenous infusion.		Administered TAK-788	Given in Combination With Pemetrexed/ Carboplatin Assessed by Adverse Events, Toxicity Grades, and Laboratory Test Results	

[a]A Phase 1/2 Study of the Safety, Pharmacokinetics, and Anti-Tumor Activity of the Oral EGFR/HER2 Inhibitor TAK-788 (AP32788) in Non-Small Cell Lung Cancer

Opmærksomhedspunkter identificeret af Horizon Scanning

Der skal anvendes en diagnostisk test forud for behandling med mobocertinib:

The FDA simultaneously approved Thermo Fisher Scientific's Oncomine Dx Target Test as an NGS companion diagnostic for EXKIVITY to identify NSCLC patients with EGFR Exon20 insertions. NGS testing is critical for these patients, as it can enable more accurate diagnoses compared to polymerase chain reaction (PCR) testing, which detects less than 50% of EGFR Exon20 insertions.
https://www.takeda.com/takeda-exkivity-mobocertinib-approved-by-us-fda/

Hovedkilder til orienteringen

1. https://www.sps.nhs.uk/medicines/
2. http://www.ema.europa.eu/
3. https://www.cancer.gov/publications/dictionaries/cancer-drug/
4. https://www.accessdata.fda.gov/mobocertinib
5. https://www.takeda.com/
6. https://medicinraadet.dk/
7. https://www.sundhed.dk/sundhedsfaglig/laegehaandbogen/
8. https://clinicaltrials.gov/

Teksten i dokumentet er kopieret fra de angivne kilder, derfor fremstår teksten på både dansk og engelsk.

Ansvarlig: Senior analytiker Anne-Mette Ørkild Mud, Amgros