Ivosidenib for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy. A Budget Impact Analysis in Greece.

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Background

- Cholangiocarcinoma (CCA) is a highly lethal, epithelial cell malignancy [1]. CCA is part of a group of biliary tract cancers that accounts approximately for 20% of all primary liver cancers and 3% of all gastrointestinal (GI) tumors [2-3].
- Given the poor prognosis in patients with advanced/metastatic CCA and the lack of effective options in the treatment of second or third line CCA, there is a substantial unmet need for effective and well tolerated treatments which extend survival [4-5].
- Treatment options for patients with previously treated, unresectable, locally advanced, or metastatic CCA with IDH1 mutations are limited to older palliative chemotherapy regimens that yield suboptimal benefit, with low response rates and rapid progression [4-5].
- Ivosidenib is an innovative, oral treatment with a first-in-class mode of action, which specifically targets and inhibits mutated IDH1 activity, limiting cell proliferation [6].
- In Europe, Ivosidenib was designated as an orphan medicinal product EU/3/18/1994 on 21 March 2018 in the following condition: treatment of biliary tract cancer [7]. On 23 February 2023, the Committee for Medicinal Products for Human Use adopted a positive opinion recommending the granting of a marketing authorization for the medicinal product Ivosidenib for the treatment of adult patients with locally advanced or metastatic CCA with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy [6].

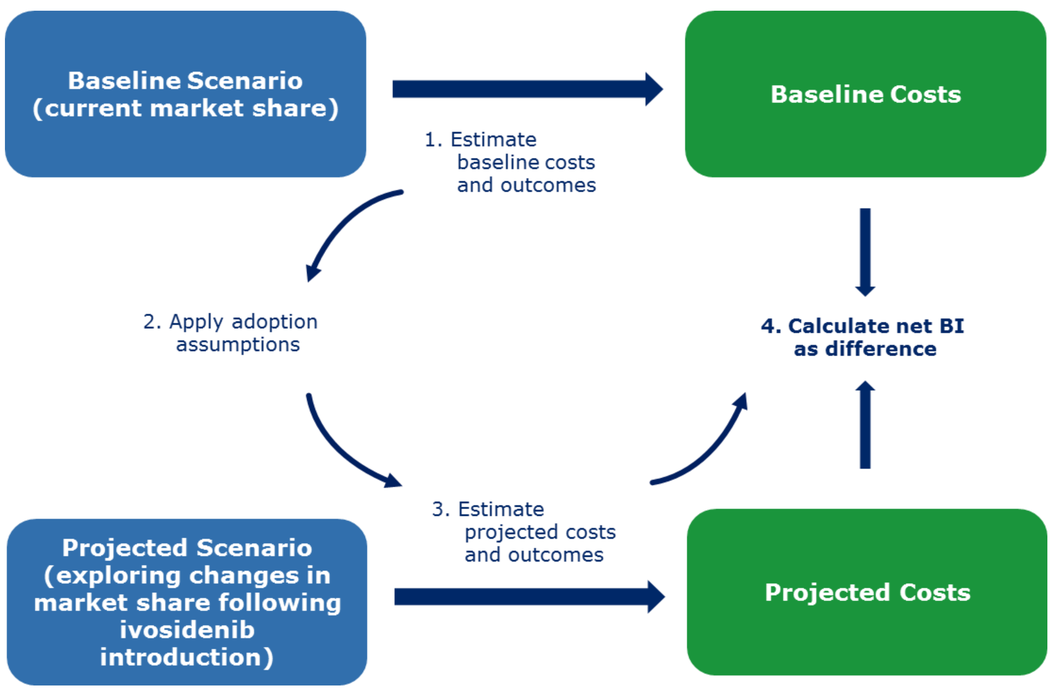
Objective

The aim of the study was to estimate the budget impact from the introduction of Ivosidenib for the treatment of patients with locally advanced or metastatic cholangiocarcinoma (CCA) with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy in Greece.

Methods

- A budget impact model (BIM) was locally adapted from a public payer perspective over a 5-year time.
- The BIM uses a traditional structure in which a " current scenario: world without Ivosidenib" reflecting the current market situation is compared to "future scenario: world with Ivosidenib in which Ivosidenib has been introduced for treatment of advanced, or metastatic CCA patients with an IDH1 R132 mutation (Figure 1).

Figure 1: Budget impact model structure



- The number of eligible patients was estimated using epidemiological data from published literature [8-12] (Table 1) while the projected uptake of Ivosidenib was provided by Servier Hellas. Ivosidenib could potentially take market share (future scenario) away from oxaliplatin-L-folinic-acid-fluorouracil (FOLFOX) and best supportive care (BSC).
- Cost inputs in the model include, drug acquisition cost (Drug list price) as they were published in the bulletin issued on 19-March-2024 by the Greek Ministry of Health [13] , while the other healthcare unit costs such as administration, monitoring, adverse events and end of life care were retrieved from published studies [14-15]. All costs reflect the year €,2024.
- The model measured outcome was incremental budget impact from the introduction of Ivosidenib as a treatment option in Greek patients with an IDH1 R132 mutated CCA.

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Table 1: Epidemiological data and market shares of current &future scenarios considered in the model

Epidemiological data	Value	Number of patients	Source
▶ Incidence of liver cancer All primary liver tumors	1,669	-	According to latest European Cancer Information System, 2022 [8]
▶ Patients with CCA Incidence of CCA (%)	20%	334	Banales et al. 2020 [9] & EMA orphan designation doc (tibsovo): 15% - 26% of all primary liver cancers
▶ Patients with iCCA Incidence of iCCA (%)	34%	113	Based on Lamarca et al. 2020 [10] : 34% of CCA patients are iCCA
▶ Patients with advanced iCCA Incidence of advanced iCCA (%)	70%	79	Valle JW et al. 2016 [11]
▶ Patients with mIDH1 Incidence of IDH1 mutations	16.5%	13	Boscoe et al (2019)[12]: 16.5% of iCCA patients with IDH1 mutations
▶ Patients eligible for 2L therapy Percentage receiving 2L therapy (%)	75%	10	Data on file-model calculations
Market shares			
Current market share scenario (without Ivosidenib)	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Best Supportive Care	50%	50%	50%	50%	50%
FOLFOX	50%	50%	50%	50%	50%
Future market share scenario (with Ivosidenib)	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Ivosidenib	30%	40%	50%	60%	70%
Best Supportive Care	40%	35%	30%	25%	20%
FOLFOX	30%	25%	20%	15%	10%

CCA: Cholangiocarcinoma; IDH1: isocitrate dehydrogenase., FOLFOX:Oxaliplatin-L-folinic-acid-fluorouracil

Results

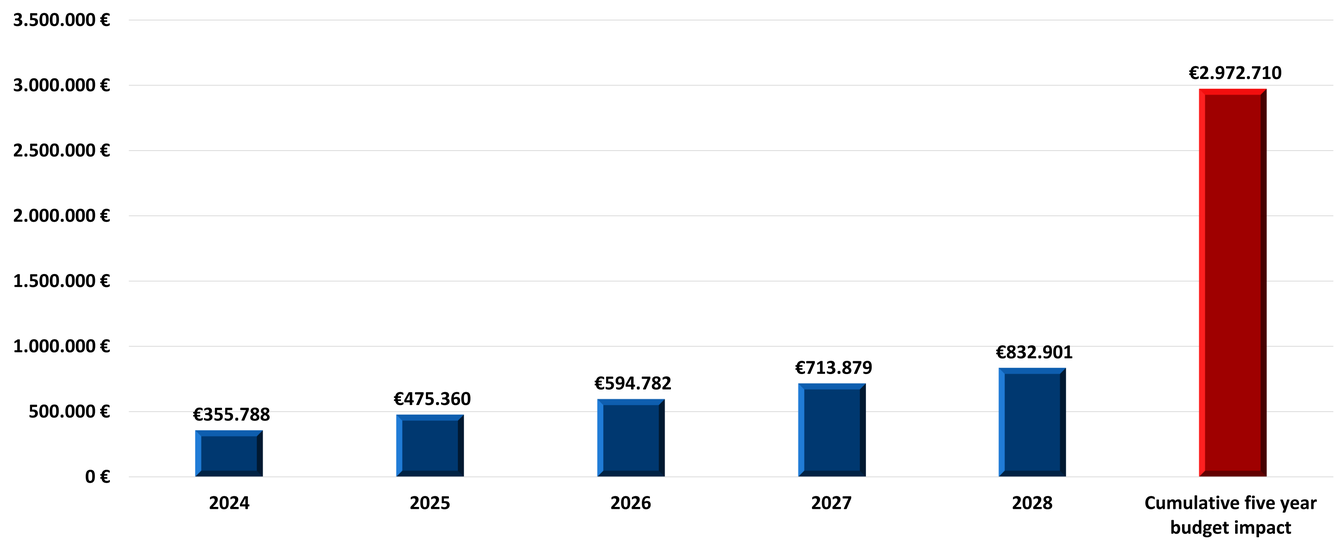
- Over the 5-year horizon, considering a constant incident number of eligible Greek patients per year, the corresponding Ivosidenib market shares were 30% in first year, 50% in third year and 70% in fifth year and the respective total expenditure increases were €355,788, €594,782 and €832,901(Table 2).

Table 2: Base case budget impact analysis results

	Year 1	Year 2	Year 3	Year 4	Year 5
Current market share scenario (without Ivosidenib)					
Total cost	€39,973	€39,973	€39,951	€39,749	€38,246
Future market share scenario (with Ivosidenib)					
Total cost	€395,761	€515,331	€634,733	€753,628	€871,148
Annual incremental cost of introduction of ivosidenib	**€355,788**	**€475,360**	**€594,782**	**€713,879**	**€832,901**

- Using in the model analysis the published drug list prices, the cumulative budget impact over 3 and 5 years was calculated at €1,425,930 and €2,972,710 respectively (Figure 2).

Figure 2: Annual and cumulative budget impact introduction of ivosidenib in the market



Conclusions

The severity of CCA, in combination with the limited number of effective treatments, results in a high level of unmet need. The advent of Ivosidenib has brought a new on-label treatment option with increased clinical benefits, and a limited budget impact for the Greek payer.

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