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Assessing the Impact of Introducing Mavacamten for the Treatment of Obstructive HCM on the Modelled System and Societal Level Burden in China

Han Bao,¹ Yu Jia,² Michael Hurst,³ Zoe Cheah,⁴ Melissa Ho,⁴ Jianwei Xuan¹

¹Sun Yat-Sen University, Guangzhou, China; ²Bristol Myers Squibb, Shanghai, China; ³Bristol Myers Squibb, Uxbridge, UK;

⁴Open Health HEOR and Market Access UK

Background

- Hypertrophic cardiomyopathy (HCM) is a complex and multifactorial myocardial disorder characterised by primary left ventricular (LV) hypertrophy ¹⁻³ and can be sub-categorized as obstructive or non-obstructive HCM by the presence of ventricular outflow tract obstruction.
- Patients with the obstructive HCM subtype are often symptomatic; typical symptoms include dyspnoea, chest pain, palpitations and syncope.⁴
- Obstructive HCM is a rare cardiovascular condition that is diagnosed in approximately 20,000 patients in China, of which approximately half (~10,000) are symptomatic (defined as New York Heart Association [NYHA] functional class II and III).
- Mavacamten is a first-in-class, small-molecule, selective allosteric inhibitor of cardiac myosin ATPase that has been developed to target the underlying pathophysiology of HCM, thus reducing contractility and improving myocardial energetics.⁵
- EXPLORER-CN (NCT05174416) is a phase III, multicentre, randomised, double-blind, placebo-controlled registration trial that evaluated the efficacy and safety of mavacamten in Chinese adults with symptomatic (NYHA class II-III) obstructive HCM.⁶
- Results from EXPLORER-CN showed that treatment with mavacamten + standard of care (SoC; including beta blocker (BB) or calcium channel blocker (CCB)) was associated with improvements in Valsalva left ventricular outflow tract (LVOT) gradient, LV filling, and NYHA functional class from baseline to week 30 compared to placebo + BB/CCB monotherapy.

Objectives

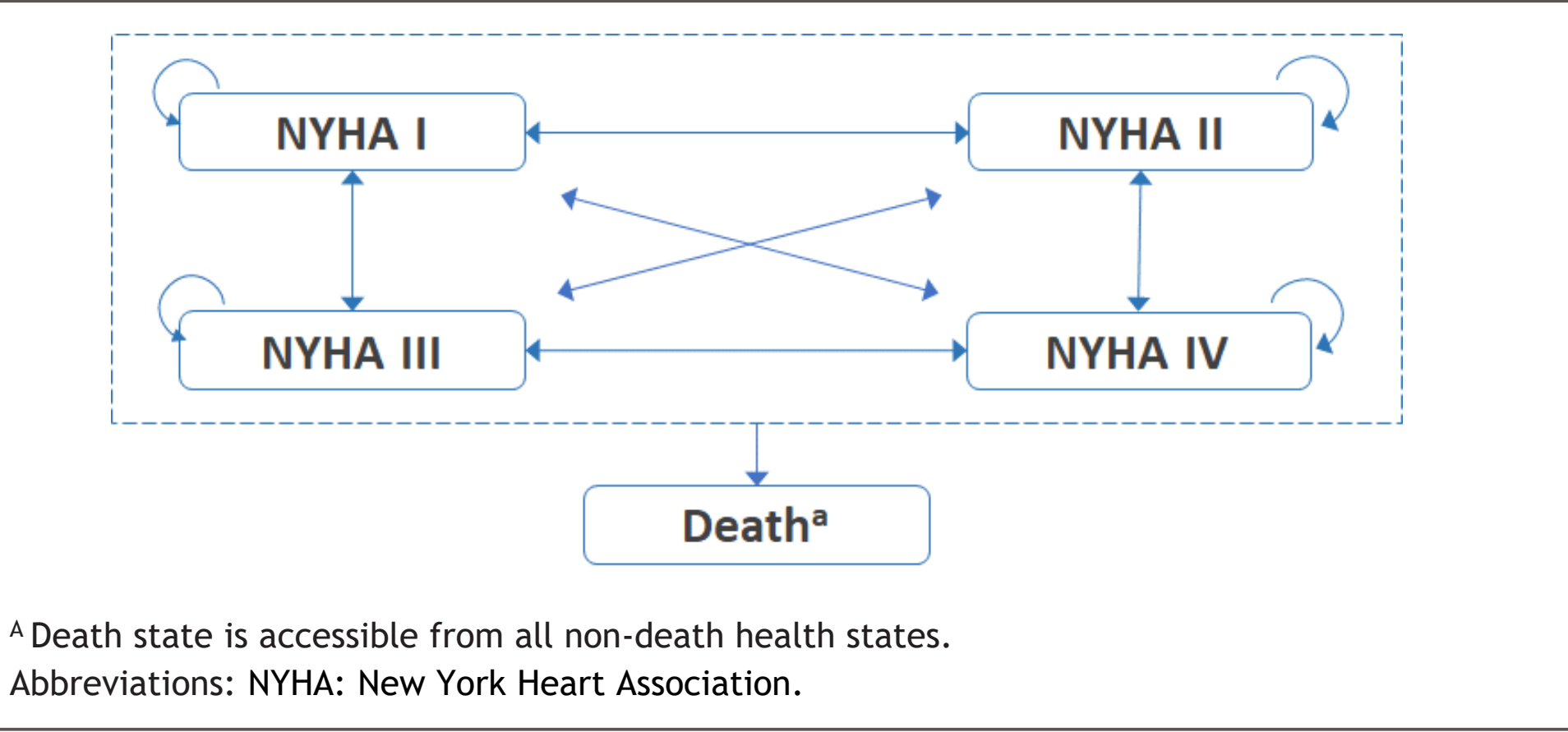
- This study aims to assess the economic impact of mavacamten + BB/CCB versus placebo + BB/CCB monotherapy to patients from Chinese societal perspective.

Methods

Model structure

- A five-state (NYHA functional class I, II, III, IV, and death) Markov model was developed with a Chinese societal perspective (**Figure 1**).
- At each cycle/assessment period, patients can remain or transition to any other NYHA health state, depending on the probability of experiencing improvement or worsening of NYHA class driven by transition probabilities. Patients are at risk of death in each model cycle.

Figure 1. Model schematic



- To align with EXPLORER-CN assessment timepoints, cycle length was varied in the first 30 weeks of the model (herein referred to as the short-term), with a subsequent fixed cycle length of 28 days to align with the anticipated dosage of mavacamten.
- To account for transitions occurring at times within a cycle, a half-cycle correction was implemented within the economic model.

Treatment sequencing

- Patients either start on mavacamten + BB/CCB or on placebo + BB/CCB monotherapy in the model.
- When patients discontinue mavacamten, the model assumes (supported by clinical guidelines and local clinical insights) they are subsequently treated with BB/CCB monotherapy.
- Mavacamten treatment discontinuation in the short term occurs at week 30 if patients experienced no improvement in NYHA class, or a serious adverse event, with rates obtained from EXPLORER-CN.
- In the long-term (post week 30), discontinuation of mavacamten is triggered by a worsening in NYHA class (within a cycle) or based on predicted annual serious adverse events, validated by clinical experts.
- For any patient in receipt of BB/CCB monotherapy (regardless of arm), the model included treatment sequencing as suggested by local experts; including potential progression to septal reduction therapies (SRTs) which was modelled as a one-off event via a tunnel condition, after which patients enter a post-SRT setting (BB/CCB only).

Model Inputs

- The starting patient population was modelled according to the baseline patient's population enrolled in EXPLORER-CN: 71.6% male, and baseline NYHA distribution of 76.54%/23.46% in NYHA class II/III, respectively; average age of 42 years based on literature was used.⁷
- Progression through and patterns of treatment were informed by transition probabilities based on EXPLORER-CN and supplemented by literature and expert opinion.
- NYHA class deterioration for all treatments was permitted through the modelling of natural disease progression, informed by literature and local expert opinion.^{8,9}
- Inputs relating to mortality for each NYHA class (II, III and IV versus I) were obtained from Wang et al. (2023)¹⁰; hazard ratio estimates were adjusted by age, gender and race based on patients with obstructive HCM in the United States (II: 1.80; III: 4.12; IV: 10.90).
- Three different types of SRTs were included in the economic model: septal myectomy (SM), alcohol ablation therapy (AAT) and ventricular septal radiofrequency ablation (VSRA).
- Treatment acquisition costs for SRTs were derived from hospital real word data and publications (internal data from Beijing Fuwai hospital).¹¹
- The proportion of patients receiving SRT was derived from a survey of 35 experienced cardiologist in China (ISPOR poster HSD13)¹² (**Table 1**).

Table 1. Proportion of patients receiving SRT, surgical costs and surgical complication costs

Inputs	SM	AAT	VSRA	Surgical complication unit cost ¥(€) ^b
SRT disposition (by procedure)	21.1%	41.4%	37.6%	-
SRT costs ¥(€)	114,200 (14,581)	80,000 (10,215)	125,200 (15,986)	-
Surgical complication				
AKI/acute renal failure (dialysis)	2.3%	0.8% ^a		66,000 (8,427)
AKI/acute renal failure (overall)	12.8%	5.3% ^a		34,143 (4,359)
Permanent pacemaker implantation	9.8%	11.3% ^a		81,396 (10,392)
Stroke	2.2%	0.5% ^a		18,017 (2,300)
Procedure cost components ¥(€)	27,048 (3,454)	37,932 (4,843)	51,395 (6,562)	-
Total weighted cost ¥(€)		116,374 (14,859)		-

Abbreviations: AAT: alcohol ablation therapy; AKI: acute kidney injury; SM: septal myectomy; SRT: septal reduction therapy; VSRA: ventricular septal radiofrequency ablation.
^a Complication rates pertaining to VSRA are assumed to be equivalent to VSRA.
^b The conversion used is based on average of 6 months data (11/03/2024 to 12/09/2024) according to European central bank; EUR 1 = CNY 7.8319.

- Health care resource use (HCRU) per year was collected via the cardiologist survey conducted in China (ISPOR poster HSD13)¹² as was indirect costs (encompassing caregiver costs and productivity loss).
- Across these three measures, patients with higher symptomatic burden (NYHA III-IV) have higher HCRU and indirect costs compared to patients with low burden (NYHA I-II).
- The HCRU costs, caregiver costs, and productivity loss costs per cycle per NYHA class are shown in **Table 2**.
- The adapted economic model represents the perspective of the Chinese healthcare system, adopting a societal perspective over a lifetime horizon. In line with Chinese guidelines, both costs and effects were discounted at 5.0% annually.

Table 2. HCRU and indirect costs per cycle

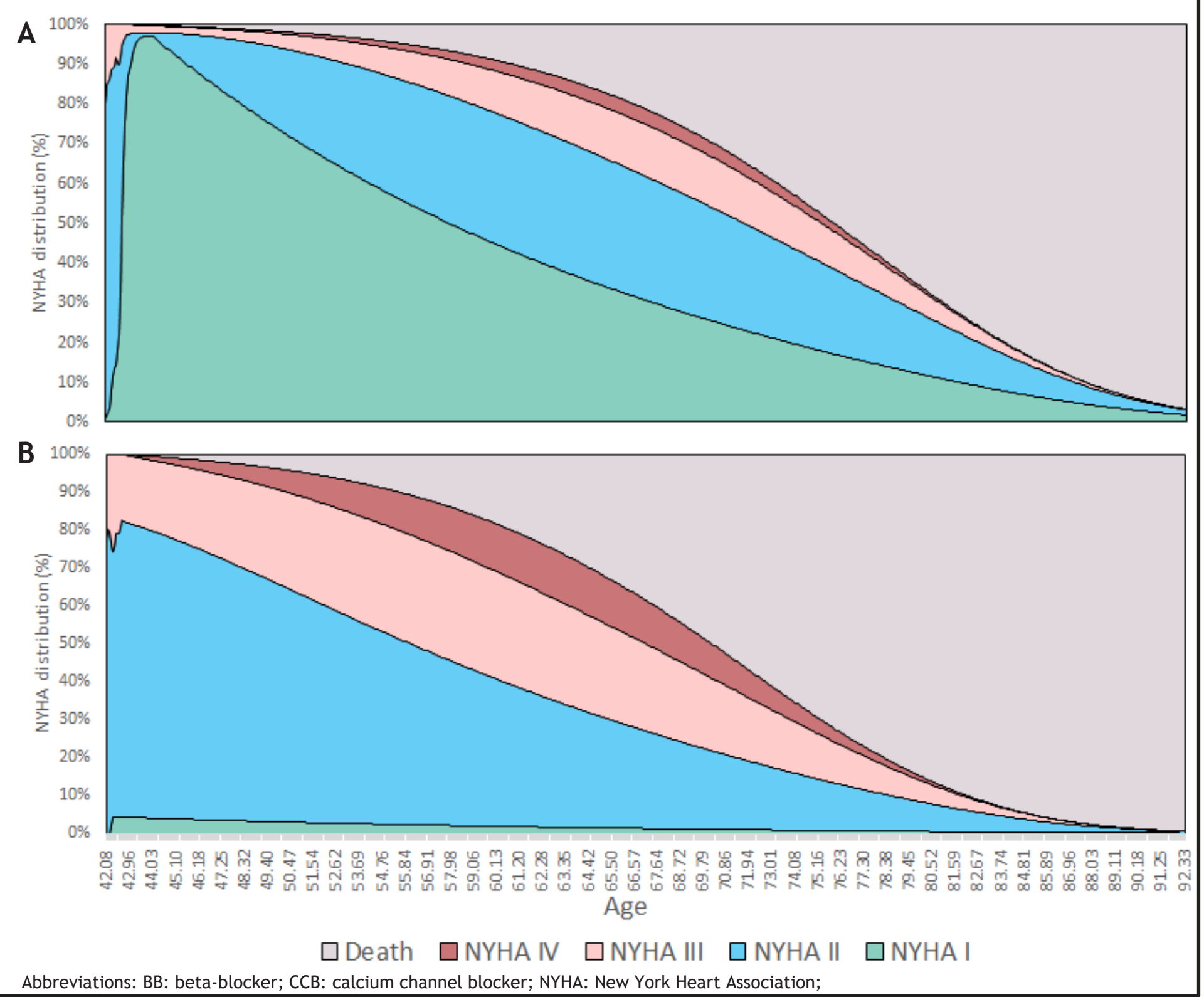
Cost category, ¥(€) per cycle	NYHA I	NYHA II	NYHA III	NYHA IV
HCRU costs	1,083 (138)	4,299 (549)	8,625 (1,101)	13,854 (1,769)
Caregiver costs	0 (0)	3,500 (447)	7,840 (1,001)	14,505 (1,852)
Productivity loss costs	176 (22)	319 (41)	572 (73)	825 (105)

Abbreviation: HCRU: health care resource use; NYHA: New York Heart Association.
^aThe conversion used is based on average of 6 months data (11/03/2024 to 12/09/2024) according to European central bank; EUR 1 = CNY 7.8319.

Results*

- * Preliminary results in the abstract were updated to reflect revisions to the modelling approach based on further clinical insights.*
- Over a lifetime horizon (50 years), patients in the mavacamten + BB/CCB arm experienced improvement in NYHA class distribution compared to placebo + BB/CCB monotherapy arm.
- More patients treated with mavacamten + BB/CCB were in NYHA class I than those treated with placebo + BB/CCB monotherapy (**Figure 2A** and **Figure 2B** respectively).

Figure 2. Health state occupancy from economic model (A: Mavacamten + BB/CCB arm; B: Placebo + BB/CCB monotherapy arm)



- The mavacamten + BB/CCB arm (vs placebo + BB/CCB monotherapy arm) produced higher modelled total life years (15.8 vs 14.4 years respectively).
- When considering a deterministic societal and payer perspective excluding treatment acquisition costs, patients treated with mavacamten + BB/CCB (vs placebo + BB/CCB monotherapy) yielded significant per-patient cost savings at ¥1,322,447 [€168,854] and ¥633,194 [€80,848] respectively (Table 3).
- Cost savings were driven by reduced costs in the mavacamten + BB/CCB arm in the following cost categories:
 - Health care resources (exc treatment) (¥596,836 [€76,206] saving)
 - Surgery costs (¥41,327 [€5,277] saving)
 - Terminal care costs (¥1,574 [€201] saving)
 - Indirect costs (¥689,252 [€88,006] saving)
- Conversely, patients within the mavacamten + BB/CCB arm had increased costs in the following cost categories:
 - Monitoring costs (¥645 [€82] increase)
 - AE costs (¥5,897 [€753] increase)
- All cost savings were driven by improved health status (depicted in the model by lower NYHA classes) whereas increases in costs were driven by additional monitoring burden of mavacamten as well as the slight increase in AE rates observed in EXPLORER-CN.

Table 3. Deterministic cost results

Cost category, ¥(€) lifetime modelled per patient	Mavacamten + BB/CCB	Placebo + BB/CCB monotherapy	Incremental costs
HCRU costs	559,350 (71,419)	1,156,186 (147,625)	-596,836 (-76,206)
BB/CCB and Surgery costs	61,390 (7,838)	102,717 (13,115)	-41,327 (-5,277)
Monitoring costs	2,843 (363)	2,198 (281)	+645 (+82)
AE costs	8,573 (1,095)	2,676 (342)	+5,897 (+753)
Terminal care costs	5,174 (661)	6,748 (862)	-1,574 (-201)
Indirect costs	398,137 (50,835)	1,087,390 (138,841)	-689,252 (-88,006)
Total costs (payer perspective)	637,330 (81,376)	1,270,524 (162,224)	-633,194 (-80,848)
Total costs (societal perspective)	1,035,467 (132,212)	2,357,914 (301,065)	-1,322,447 (-168,854)

Abbreviation: AE: adverse event; BB/CCBs: beta blockers/calcium channel blockers; HCRU: healthcare resource utilisation.
^aThe conversion used is based on average of 6 months data (11/03/2024 to 12/09/2024) according to European central bank; EUR 1 = CNY 7.8319

Conclusions

- Mavacamten + BB/CCB offers significant clinical value as patients experienced improvement in NYHA class distribution and longer life expectancy compared to placebo + BB/CCB monotherapy.
- Mavacamten + BB/CCB not only offers significant clinical value but has the potential to yield substantial economic benefits across multiple cost components compared to the current standard of care.

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- HB accepted the research funding from BMS and no other conflict of interests
- XJ has no conflict of interests
- MH and YJ are employees of BMS and may hold stock options
- ZC and MH are employees of OPEN Health, which has received consultancy fees from BMS.
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