**Clinical and economic impact of ibalizumab for people with multidrug-resistant HIV in the United States**

**Supplementary material**

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**METHODS**

**Input parameters**

*HIV transmissions*

In order to calculate transmission rates over five years, we use estimates of community viral load, produced by the model, along with viral-load specific monthly transmission rates.1 Viral load-specific transmission rates ranged from 0.16-9.03 transmissions/100 person-years (PY) and are based on a meta-analysis on transmission rates from unprotected intercourse (Supplementary Table 1)1. Based on data regarding the frequency and effectiveness of condom use in the US, we reduced transmission rates by 40% for the whole population (Supplementary Table 1).2–5

**RESULTS**

**HIV transmissions**

Transmission rates decreased from 4.81/100PY with *OBR* to 3.51/100PY with *IBA+OBR* over five years. The population in the TMB-202 analysis had more people with high viral load setpoints; because of this, transmissions in this scenario were higher in both strategies compared to the base case, decreasing from 5.33/100PY with *OBR* to 3.96/100PY with *IBA+OBR* over five years.

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| **Supplementary Table 1. Additional base case input parameters for a modeling analysis of *IBA+OBR* compared to *OBR* for people with MDR HIV in the US** |
| Parameter | Base Case Value | Reference |
| **Cohort characteristics** |  |  |
|  HIV transmission rates by viral load/100 PY  (HIV RNA copies/mL) |  | 1 |
|  >100,000 | 9.03 |  |
|  10,001-100,000 | 8.12 |  |
|  3,001-10,000 | 4.17 |  |
|  501-3,000 | 2.06 |  |
|  <500 | 0.16 |  |
|  HIV transmission reduction by condom use, % | 40 | 2 |
| **Quality of life (utility weights)**a | *IBA+OBR* | *OBR* |  |
|  Routine care, by CD4 |  |  | 7 |
|  >500/µL | 0.87 | 0.87 |  |
|  201 – 500/µL | 0.86 | 0.86 |  |
|  51 – 200/µL | 0.85 | 0.85 |  |
|  ≤50/µL | 0.83 | 0.83 |  |
|  Acute opportunistic infections |  |  | 8 |
|  Pneumocystis pneumonia | 0.74 | 0.74 |  |
|  Mycobacterium avium complex | 0.69 | 0.69 |  |
|  Toxoplasmosis | 0.69 | 0.69 |  |
|  Cytomegalovirus | 0.78 | 0.78 |  |
|  Severe fungal infection | 0.78 | 0.78 |  |
|  Other opportunistic infection | 0.69 | 0.69 |  |

***IBA+OBR***: ibalizumab and optimized background regimen treatment strategy. ***OBR***: optimized background regimen only strategy. **MDR**: multidrug-resistant. **PY**: person-year.

aQuality of life weights were derived from AIDS Clinical Trials Group studies.

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| **Supplementary Table 2.** **Clinical impact and cost-effectiveness of *IBA+OBR* compared with *OBR* for people with MDR HIV in the US** |
|  | Cohort | 5-yr survival(% alive) | Lifetime QALE (y) | Total lifetime cost (USD)a | ICER (USD/QALY)a | Transmissions/100 PY over 5yb |
| **Base case** | *OBR* | 38 | 3.74 | $301,700 | -- | 4.81 |
| *IBA+OBR* | 47 | 5.12 | $661,800 | $260,900 | 3.51 |
| **Scenario analyses** |
|  TMB-202 trialc | *OBR* | 33 | 3.21 | $276,100 | -- | 5.33 |
| *IBA+OBR* | 44 | 4.64 | $637,100 | $250,900 | 3.96 |

**Late failure:** virologic failure after 48 weeks on ibalizumab regimen. ***IBA+OBR***: ibalizumab treatment strategy. ***OBR***: optimized background regimen only strategy. **MDR**: multidrug-resistant. **QALE:** quality-adjusted life expectancy. **QALY:** quality-adjusted life year. **USD:** 2018 US dollars. **ICER:** incremental cost-effectiveness ratio. **PY:** person-year.

a Discounted 3% annually.

b Transmission rates include first-order transmissions from the initial cohort only.

c The TMB-202 trial is a phase-2b trial of ibalizumab (n = 113) and we use cohort characteristics from this trial in a scenario analysis.6

**FIGURE LEGENDS**

**Supplementary Figure 1. Probabilistic sensitivity analysis examining the cost-effectiveness of IBA+OBR compared to OBR.**

This shows the probability of each regimen being preferred, in terms of net monetary benefit ([quality-adjusted life-years]\*[willingness-to-pay] – [lifetime costs]) when varying four parameters: CD4 decline multiplier on failed ART, IBA efficacy, time between experiencing toxicity and discontinuing IBA, and quality of life decrement due to IBA toxicity. OBR is always the preferred strategy from the cost-effectiveness point below a willingness-to-pay (WTP) threshold of $250,000/QALY, and they are equally preferred at a WTP threshold of $263,000/QALY.

**Supplementary Figure 1****. Probabilistic sensitivity analysis examining the cost-effectiveness of *IBA+OBR* compared to *OBR*.**



***OBR***: optimized background regimen only strategy. ***IBA+OBR***: ibalizumab and optimized background regimen treatment strategy. **QALY**: quality-adjusted life year