Characteristics and Costs of Optimized Background Therapy for Treatment of Heavily Treatment-Experienced Adults With Multidrug-Resistant HIV-1 in the US: A Clinical Trial Analysis

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BACKGROUND

- Heavily treatment-experienced adults with multidrug-resistant (MDR) HIV-1 infection represent a difficult-to-treat population with limited remaining antiretroviral treatment options.
- Treatment guidelines recommend optimizing antiretroviral therapy based on an individual's resistance profile.[1]
  - Antiretroviral drug use and costs of optimized background therapy (OBT) are therefore implicitly individualized and likely heterogeneous.
  - However, the composition and cost of OBT are not well described in the literature.
- Phase 3 clinical trial for adults with MDR HIV-1 treated with ibalizumab-uiyk plus OBT provides a unique opportunity to better understand the characteristics and costs of OBT in this patient population.[2]
  - OBT was investigator selected and based on participants' resistance profile.
  - Trial participants (n = 40)[a] were heavily treatment experienced, with the following baseline overall susceptibility scores (OSS):
    - OSS 0: 12.5%
    - OSS 1: 30.0%
    - OSS ≥ 2: 57.5%

OBJECTIVE

- This study assesses the characteristics and cost of OBT in the United States (US) for participants in a phase 3 clinical trial for adults with MDR HIV-1 treated with ibalizumab-uiyk plus OBT.[2]

METHODS

- Descriptive statistics were used to analyze patient-level, investigator-selected OBT initiated at Day 14 (i.e., 7 days after treatment with ibalizumab-uiyk began).[b]
- Costs of individual antiretroviral drugs were applied to assumed standard dosages from US treatment guidelines[1] using wholesale acquisition costs from RedBook Online[3] (Table 1) to calculate annual OBT costs.
  - Annual costs of OBT excluded the cost of ibalizumab-uiyk and investigational drug.
  - Separate analyses were conducted using branded and generic prices (for drugs with generics available).
- Key outcomes of interest included the following:
  - Composition of OBT, including most frequent antiretroviral drugs
  - Use of fixed-dose combination (FDC) and investigational drugs
  - Number of antiretroviral drugs, by investigational drug use
  - Annual OBT costs, by investigational drug use and with and without generic drug use

[a] Note that the clinical trial included 4 participants from Taiwan; other participants were from the US.

[b] Note that investigational agent fostemsavir was considered part of initial OBT for some participants who initiated fostemsavir up to Day 21.

Table 1. Antiretroviral Drug Costs for Drugs Used in the TMB-301 Trial

Antiretroviral Drug	WAC Drug Price per Day (Generic Price[a])
FDCs	
Abacavir/dolutegravir/lamivudine	$86.63
Atazanavir/cobicistat	$53.52
Darunavir/cobicistat	$55.81
Emtricitabine/tenofovir DF	$52.25
Emtricitabine/tenofovir alafenamide	$52.25
Lamivudine/zidovudine	$30.05 ($4.45)
CCR5 antagonist	
Maraviroc	$46.66
Fusion inhibitor	
Enfuvirtide	$119.52
Integrase inhibitors	
Dolutegravir	$51.19
Raltegravir	$46.32
NNRTIs	
Etravirine	$39.21
Rilpivirine	$32.23
NRTIs	
Abacavir	$18.62 ($5.00)
Lamivudine	$13.86 ($3.88)
Tenofovir	$35.55
Investigational agent	
Fostemsavir[b]	$0.00
PIs	
Atazanavir	$48.31
Darunavir	$48.83
Fosamprenavir	$38.62
Lopinavir/ritonavir	$32.24
Ritonavir	$8.57
Tipranavir	$49.63

CCR5 = C-C motif chemokine receptor type 5; DF = disoproxil fumarate; FDC = fixed-dose combination; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; WAC = wholesale acquisition cost.

[a] Drug price for drugs with generic options available.

[b] Fostemsavir was used as an investigational drug at the time of the TMB-301 clinical trial.

Source: RedBook Online, 2017.[3]

RESULTS

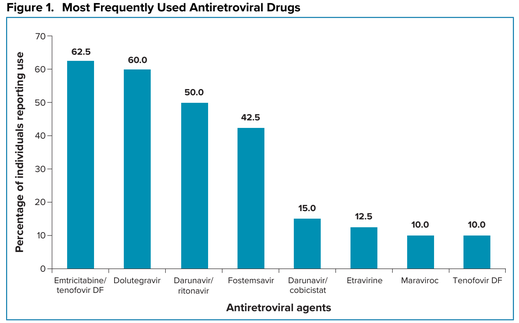
OBT Characteristics

- Among trial participants, the most frequent antiretroviral drugs used as part of OBT are shown in Figure 1.
- Excluding ibalizumab-uiyk, OBT consisted of 4.7 antiretroviral drugs (range: 1-7), with more drugs used by those treated with an investigational agent (mean: 5.5; range: 3-7) than by those not treated with an investigational agent (mean: 4.0; range: 1-6) (Table 2).
- Few participants' OBT regimens included drugs with generic options available (7.5%).
- All protease inhibitors included in OBT regimens (n = 32) were boosted, as recommended by US treatment guidelines.[1]
- As part of OBT, 85% of participants used ≥ 1 (range: 0-2) FDC drug.

Cost of OBT

- Assuming branded prices, the mean annual cost of OBT was $51,551 (Figure 2).
- Annual OBT costs were higher among those treated with an investigational agent (mean: $56,797) than among those not treated with an investigational agent (mean: $47,673) (Figure 2).
- For clinical trial participants whose OBT regimens included drugs with generic options available, costs of OBT were 6%-41% lower if generic options were used; however, OBT costs with generic drugs were only 0.9% lower, on average, because only 7.5% of clinical trial participants had OBT regimens that included drugs with generic options available (Figure 2).

Figure 1. Most Frequently Used Antiretroviral Drugs



DF = disoproxil fumarate; FDC = fixed-dose combination; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor.

Note: Ritonavir was used by 57.5% of clinical trial participants. All other antiretroviral drugs were used in < 10% of clinical trial participants.

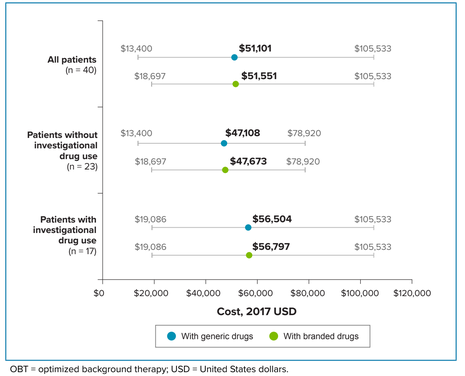
Table 2. Characteristics of Patient-Level OBT

Population	All Patients	Patients With Investigational Drug Use	Patients Without Investigational Drug Use
Number of patients	**40**	**17**	**23**
Number of ARVs in OBT[a]			
N	187	94	93
Mean	4.7	5.5	4.0
Range	1.0-7.0	3.0-7.0	1.0-6.0
Number (%) of patients taking FDCs			
N	34	16	18
%	85.0%	94.1%	78.3%

ARV = antiretroviral; FDC = fixed-dose combination; OBT = optimized background therapy.

[a] When FDCs were used, each agent within the FDC was counted separately. Boosting agents (i.e., ritonavir, cobicistat) were also counted separately.

Figure 2. Mean Annual Cost of OBT



OBT = optimized background therapy; USD = United States dollars.

Notes: Mean annual cost of OBT as well as minimum and maximum annual costs are shown in 2017 USD. Costs of investigational drugs were not included in analyses. Median annual costs of OBT (not shown in figure) were $52,714 for all patients, $61,787 for patients with investigational drug use, and $47,778 for patients without investigational drug use and did not differ for analyses with and without generic drug costs.

LIMITATIONS

- Antiretroviral drug use is based on data from the TMB-301 clinical trial and thus represents prescribing patterns and OBT in a controlled clinical trial setting. Characteristics of OBT and costs may therefore not be generalizable to real-world OBT use.
- Clinical trial data were not available on branded vs. generic drug use.
- Analyses were limited to the antiretroviral drugs used and did not include analysis of dosing, dose intensification, or use of recycled agents as part of OBT.

DISCUSSION

- Results from this study highlight the wide range in antiretroviral agents used in OBT and OBT costs for heavily treatment-experienced adults with MDR HIV-1 infection.
- Annual costs of OBT were generally high (> $50,000 per year) but varied widely across patients.
  - Annual costs were higher among individuals using investigational drugs, despite the assumed $0 costs of investigational drugs used in analyses. These results likely reflect investigational drug use with a higher number of antiretroviral agents included in their OBT on average compared with individuals without investigational drug use (5.5 vs. 4.0, respectively).
  - Although generic drug use resulted in reduced annual costs of OBT, few OBT regimens included drugs with generic drug options available.
- A previous randomized controlled trial (OPTIMA) found that intensive regimens (with ≥ 5 antiretrovirals) were not associated with clinical benefit or harm as compared with standard regimens (with ≤ 4 antiretrovirals) in the advanced MDR population.[4]
  - In the TMB-301 clinical trial population, some patients received intensive regimens, which may have led to high drug costs. Costs may be a factor when considering treatment optimization for individuals with MDR HIV-1 in real-world practice.
  - Recommendations related to the use of intensive regimens or mega-HAART are not clear in the US treatment guidelines.[1]
- Given the heterogeneity in OBT composition and associated costs, future economic analyses that include costs of OBT should consider testing the ranges of OBT costs.
- Given the limited remaining treatment options for individuals with MDR HIV-1 infection, new, potent therapies with a new mechanism of action are needed for this patient population.

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DISCLOSURE

Funding for this study was provided by Theratechnologies, Inc.

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