

The Road to an HIV Cure: Approaches and Strategies in Current Clinical Trials

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SUMMARY

- This review examined the current clinical trial landscape as it relates to the treatment and cure of HIV.
- The most common targets in current HIV clinical trial research were therapeutic vaccines, combination treatments, antibodies, treatment intensification and early treatment, gene therapies, latency reversing agents, and immune checkpoint inhibitors.
- While many treatment strategies are currently under investigation, they are primarily in the early stages of development.

CONCLUSIONS

- The findings of this review exemplify the HIV cure landscape as it evolves over the next 5-10 years.
- The ultimate treatment for HIV may involve any of the identified strategies alone or in combination.
- Understanding the current state of this research, the treatment populations, and outcomes is key to understanding whether the HIV cure pipeline is built for success.

BACKGROUND

Introduction

- Approximately 39 million people worldwide currently have HIV, 37.5 million adults and 1.5 million children.¹
- The first antiretroviral therapy (ART) for HIV, azidothymidine (AZT) - a nucleoside reverse transcriptase inhibitor (NRTI), was approved in 1987.²
- Development of additional ARTs through the end of the 20th century included protease inhibitors (PI)s, non-nucleoside reverse transcriptase inhibitors (NNRTI)s, and combination treatment termed highly active antiretroviral therapy (HAART). Subsequently, entry inhibitors, integrase inhibitors, and long-acting ARTs came on the market.²
- The goal of ART treatment has remained unchanged in 3 decades, to suppress viral load, to restore immune function, and to improve quality of life.²
- Current therapeutic approaches to curing HIV include stem cell transplantation, gene editing, therapeutic vaccines, broadly neutralizing antibodies, and immune-based therapies.
- While pharmacological advances for treating HIV have been at the forefront of science and have allowed individuals with HIV to live healthy lives without viral transmission, there remains no effective cure for HIV.
- The ongoing global burden of new HIV infections, the rise in treatment resistance, and other limitations of current treatment strategies highlight the need for a cure for HIV.³

Study Objective

- The purpose of this landscape review was to leverage information on current and recently completed clinical trials relating to HIV treatment strategies and cure.

METHODS

- Data on current and recently completed clinical trials was obtained from the report of the HIV advocacy organization The Treatment Action Group (TAG) (<https://www.treatmentactiongroup.org/>).
- TAG provides a listing of clinical trials and observational studies related to the research effort to cure HIV infection, mainly derived from the clinicaltrials.gov online registry.
- Studies reviewed here date from January of 2018 to June of 2023.
- Clinical trials were stratified by completion status, treatment target, and phase of study. Observational studies were not included.

RESULTS

- A total of 294 clinical trials for which phase of treatment was available were examined. Of these, 77 (26.2%) were current and 217 (73.8%) were recently completed.
- TAG identified 32 research targets for HIV studies. The results highlight the 7 most common targets: Therapeutic Vaccines (19.7%), Combination Treatment (14.3%), Antibodies (13.3%), Treatment Intensification/Early Treatment (9.2%), Gene Therapies (9.2%), Latency Reversing Agents (5.1%) and Immune Checkpoint Inhibitors (3.7%) (**Table 1**).

Table 1. HIV Current and Completed Clinical Trials by Target

TARGET	STUDIES	%
Adoptive Immunotherapy	7	2.4%
Analytical Treatment Interruption	1	0.3%
Anti CMV Therapy	1	0.3%
Antibodies	39	13.3%
Anti-Fibrotic	4	1.4%
Anti-Inflammatory	5	1.7%
Anti-Proliferative	1	0.3%
Antiretroviral Therapy	8	2.7%
Assembly Inhibitors	2	0.7%
BCL-2 Antagonists	1	0.3%
Cannabinoids	2	0.7%
Combinations	42	14.3%
Cytokines	4	1.4%
DART Molecules	2	0.7%
Gene Therapies	27	9.2%
Gene Therapies for People with Cancer	6	2.0%
GnRH Agonists	1	0.3%
Hormones	1	0.3%
Imaging Studies	4	1.4%
Immune Checkpoint Inhibitors	11	3.7%
Immunomodulators	1	0.3%
Iron Chelators	1	0.3%
Janus Kinase Inhibitors	2	0.7%
Latency Reversing Agents	15	5.1%
mTOR Inhibitors	4	1.4%
Proteasome Inhibitors	1	0.3%
Stem Cell Transplantation	5	1.7%
Stimulants	1	0.3%
T-Cell Receptor-Based Bispecifics	2	0.7%
Therapeutic Vaccines	58	19.7%
Toll-Like Receptor Agonists	5	1.7%
Traditional Chinese Medicine	1	0.3%
Treatment Intensification/Early Treatment	27	9.2%
Tyrosine Kinase Inhibitors	2	0.7%

- The remaining targets account for the remaining 25.5% of studies (**Figure 1**).
- Approximately 90% of the trials were Phase I or II, with the proportion evenly split between the two. Only 10% of the trials were Phase III or Phase IV (**Figure 2**).
- Examining the phases of research for each of the highlighted targets shows that except for Treatment Intensification/Early Treatment, nearly all studies were in the early Phase I or II of development (**Figure 3**).

Figure 1. HIV Clinical Trials by Highlighted Target

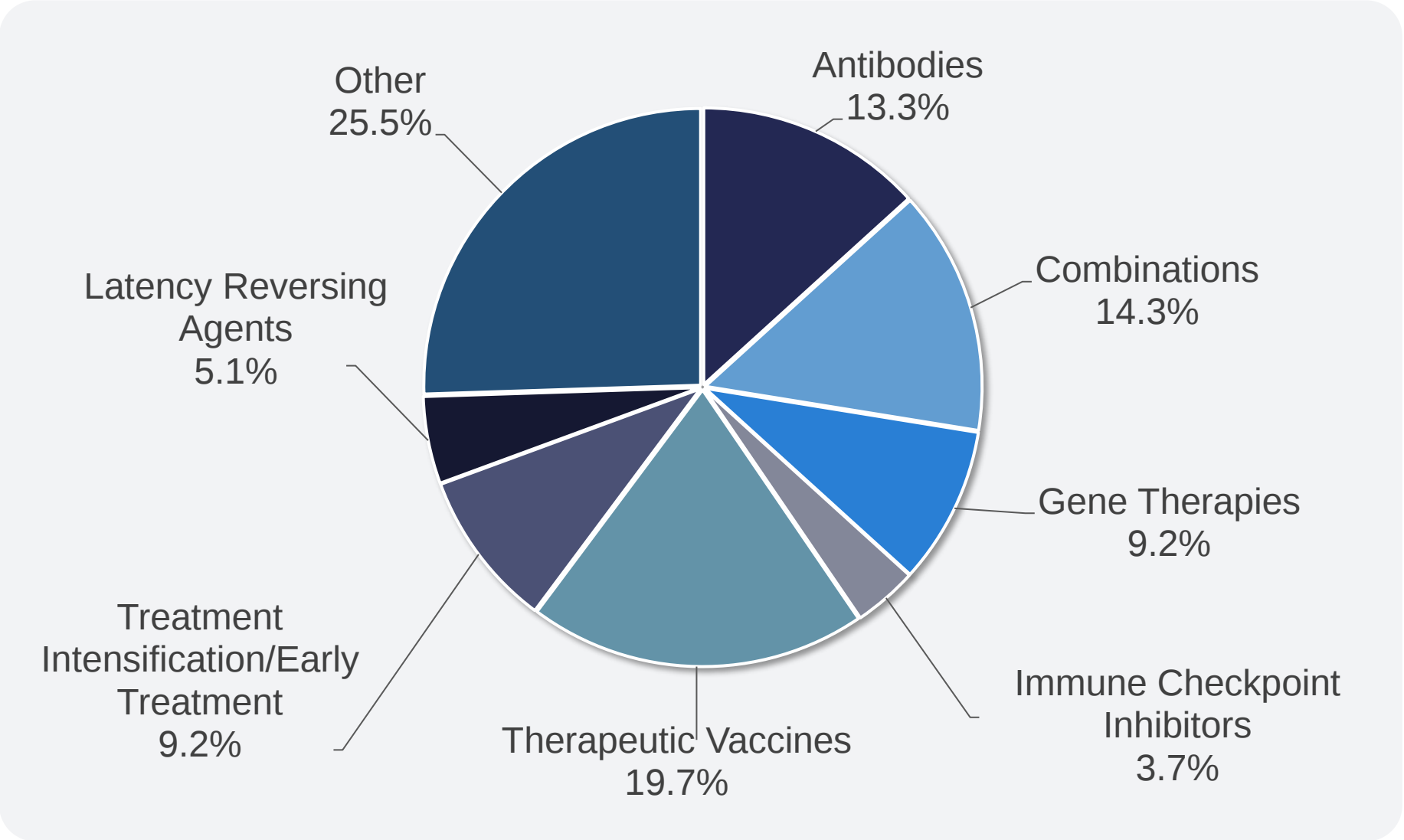


Figure 2. HIV Clinical Trials by Phase of Research

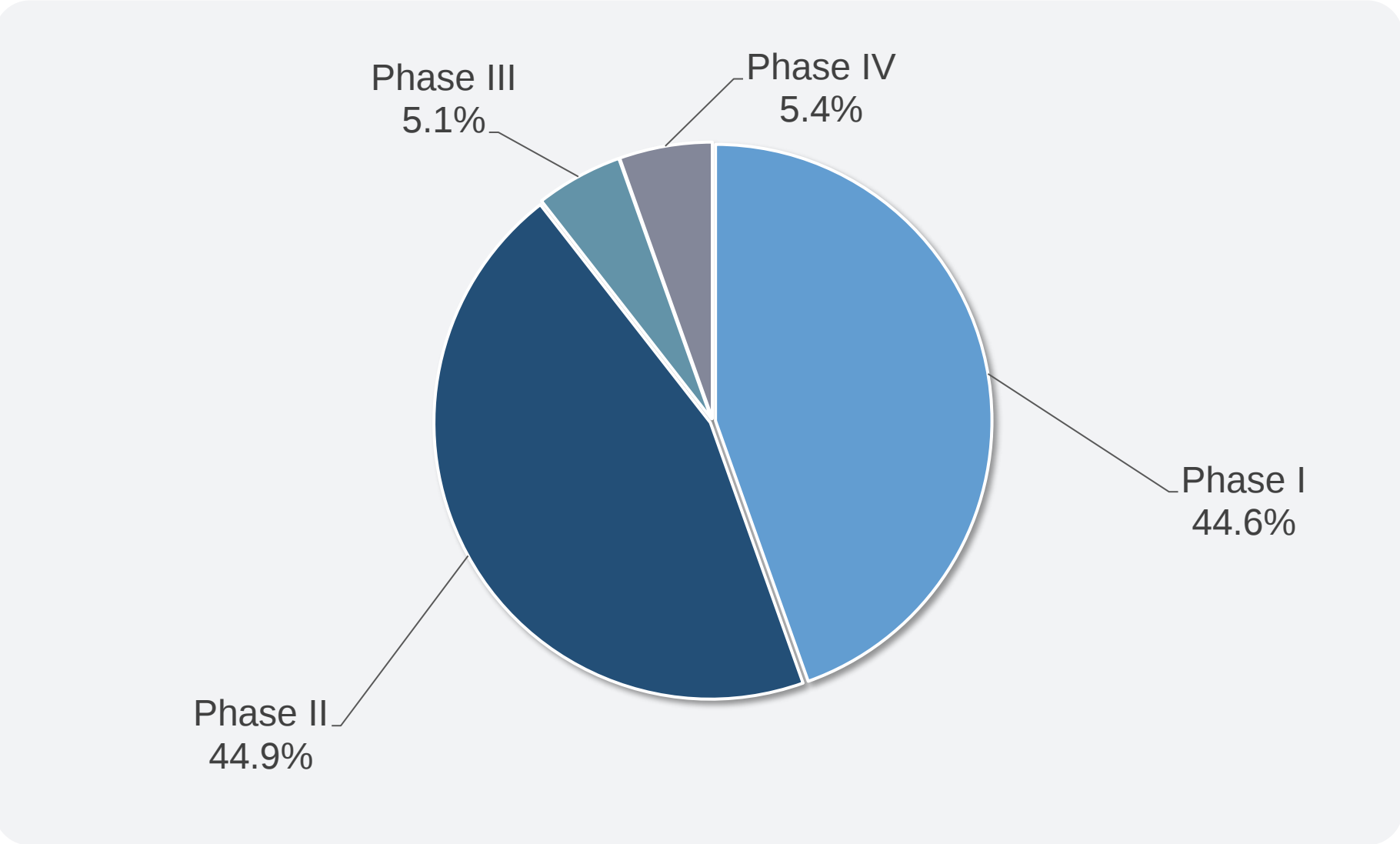
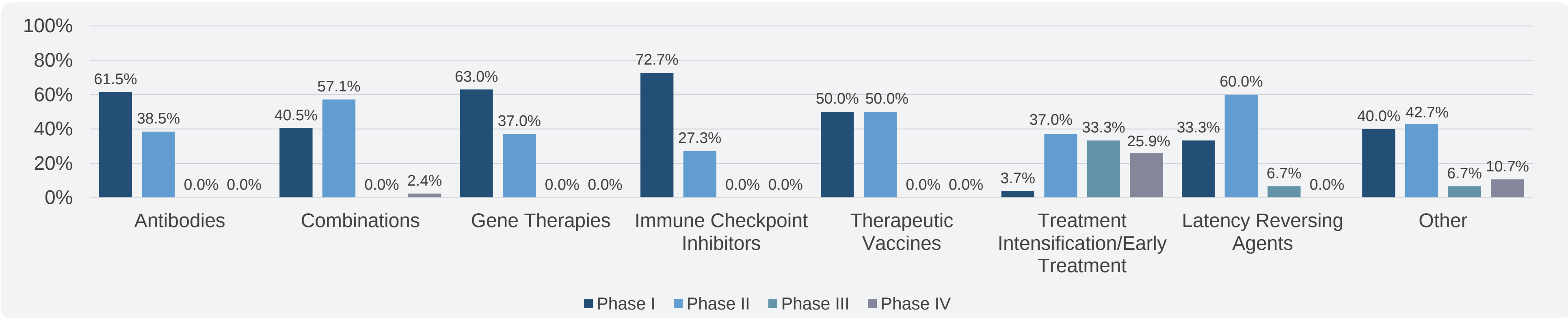


Figure 3. Phase of Research by Highlighted Target



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