

# Supplementary Online Content

Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society–USA Panel. *JAMA*. doi:10.1001/jama.2018.8431

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This supplementary material has been provided by the authors to give readers additional information about their work.

## eMethods: Recommendations Development Process

### I. Brief Summary

The recommendations for antiretroviral therapy in adults with HIV infection recommendations were developed by an international panel of experts in HIV research and patient care. The Panel was established initially in 1995 by the International Antiviral Society–USA (IAS–USA)<sup>1</sup>; members are selected by the IAS–USA Board of Directors and vetted by the organization for suitability for the panel. Panel members serve in a volunteer (uncompensated) capacity and do not participate in industry promotional activities such as speakers' bureaus, paid lectures directly for industry, or other marketing activities during their tenure on the panel. Members of the current panel convened in person and by conference calls from October 2017 to June 2018. The chair (Michael S. Saag, MD) oversees the discussions of the process and evidence review and manuscript development, and guides the group to consensus. Section leaders (**eBox 3**) and teams were appointed to evaluate evidence and summarize panel discussions for each section. Prior to selection of the section teams and leaders, panel members declared their financial relationships with commercial concerns, discussed potential conflicts of interest (COIs), and recused themselves from serving as section leaders or team members as necessary.

Evidence considered for updating the recommendations was limited to data published in the scientific literature, presented at major peer-reviewed scientific conferences, or released as safety reports by regulatory agencies or data safety and monitoring boards, since the last update in 2016 through February 2018.<sup>2</sup> Monthly literature searches are conducted by a systematic review methodologist at the University of California San Francisco. Each monthly publication list is reviewed by a panel member (Paul A. Volberding, MD) for relevance. Approximately 237 citations were ultimately identified from a list of more than 4490 over the 20 months. Relevant abstracts publicly presented at recent scientific conferences were identified by panel members. Manufacturers of antiretroviral drugs were asked to submit lists of relevant publications or abstracts meeting the established criteria. All reference lists, published papers, abstracts, and other relevant reports were organized and stored on a web-based, shared, electronic drive to which all panel members have ongoing access.

These recommendations focus on HIV-1–infected adults in international, developed-world settings where antiretroviral drugs are generally available (approved by regulatory bodies or available by expanded access) or in late-stage development (new drug application filed). Recommendations were made by full-panel consensus and rated according to the strength of the recommendation and the quality of the supporting evidence (**Manuscript Table 1**). For areas in which recommendations have not changed substantially or no or few new data are available, the reader is referred to the previous report.<sup>3</sup>

### II. Detailed Summary

#### a. Background

The medical management of HIV changes rapidly, owing to the continued rapid advances in pathogenic and clinical knowledge leading to necessary changes in patient care, as well as ongoing availability of new drugs, formulations, and laboratory testing to optimally manage HIV infection. In 1995, on recognizing the rapidly changing knowledge base, the complexity of HIV management and expertise needed to provide quality care, and the lack of current plans to update any existing HIV guidelines, the need to disseminate reliable evidence-based guidance for clinicians involved in HIV management was clear. The IAS–USA International Antiretroviral Recommendations Panel was established in 1995 by the IAS–USA to develop this needed guidance for physicians and other clinicians actively involved in HIV care.

#### b. The IAS–USA and Its Role in the Recommendations

The IAS–USA is a 501(c)(3) not-for-profit, mission-based, nonmembership, educational organization that was established in 1992. The mission of the IAS–USA is to improve the treatment, care, and quality of life for people with HIV, hepatitis C virus (HCV), or other viral infections through high-quality, relevant, balanced, and needs-oriented education and information for practitioners who are actively involved in medical care. The IAS–USA delivers annual continuing medical education (CME) programs on HIV and HCV that include live courses; live intensive, interactive workshops; live webinars; online interactive activities in the series *Cases on the Web (COW)*; and the peer-reviewed, indexed

journal *Topics in Antiviral Medicine*.™ In addition, IAS–USA manages and serves as the CME sponsor for the annual HRSA-supported Clinical Conference for Ryan White HIV/AIDS Program Practitioners, and for the annual Conference on Retroviruses and Opportunistic Infections (CROI), a research conference.

The IAS–USA is accredited *with commendation* by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

IAS–USA has sponsored the development of evidence-based recommendations for viral load monitoring, antiretroviral therapy, HIV drug resistance testing, cytomegalovirus (CMV) infection, and the metabolic complications of antiretroviral therapy, all of which are published in the medical literature.<sup>1,4-20</sup> In addition to the published recommendations, the IAS–USA served as the collaborating partner for the American Association for the Study of Liver Diseases (AASLD)/Infection Diseases Society of America (IDSA)/IAS–USA HCV Guidance ([www.HCVguidelines.org](http://www.HCVguidelines.org)) from its inception until January 2016.

The volunteer members of the IAS–USA Board of Directors (**eBox 1**) oversee the development of the information and educational programs and are not compensated for their roles in oversight and governance of the organization.

IAS–USA funding comes from a variety of sources. Largest single source of revenue is conference and CME participant registration fees. Other funding sources include grants from the pharmaceutical/diagnostics (commercial) industries, grants and subcontracts from government agencies, private donations, and gifts-in-kind from local community businesses and individuals. The commercial support that IAS–USA accepts is only for selected activities. Two large national CME efforts (one on HIV and another on HCV) invite funding in the form of educational grants from industry. Per IAS–USA policy, any effort that uses commercial grants must receive grants from several companies with competing products. Funds are pooled and distributed to activities within the effort at the sole discretion of the IAS–USA. Funders have no input into any activity, including its content, development, or selection of topics or speaker(s). Funders are listed in each activity as applicable.

The development of the Antiretroviral Therapy Recommendations is supported and funded by the IAS–USA. The IAS–USA determined the need for updated recommendations; selected panel members based on expertise in research and care to represent developed-world settings affected by HIV disease; determined the most appropriate way in which to disseminate the information (eg, publication in a medical journal rather than publication in the IAS–USA journal, web publication, etc); and provided administrative oversight and financial support.

The Panel itself is responsible for proposing the design and conduct of the work; collection, management, analysis, and interpretation of the data; and preparation, review, and approval of the manuscript. IAS–USA provided staff support for administrative management, oversight of literature searches and editorial and production assistance. At least one member of the Board serves in each panel to ensure continuing with the IAS–USA mission.

### **c. Identifying and Screening Panel Members**

The panel was initially appointed in 1995, and members have rotated periodically since then. In evaluating potential participants for the Panel, the IAS–USA Board considered individuals who 1) are recognized as authorities in HIV treatment research and clinical care, 2) have appointments in major medical teaching or research institutions, 3) have a demonstrated ability to review and evaluate evidence in an effort to provide useful recommendations in the field, 4) meet the IAS–USA COI and financial relationship criteria for participation (see below and [www.iasusa.org](http://www.iasusa.org)), and 5) have the ability to work in a collaborative consensus process. In addition, the Board emphasized the need for an international, developed world perspective.

Like the IAS–USA Board of Directors, participants in IAS–USA panels are volunteers and receive no financial compensation for their panel participation. In joining the Panel, members agree to commit substantial time to the effort necessary for evidence review and for participation in the consensus process.

### **d. COI Management**

It is the policy of IAS–USA to ensure balance, independence, objectivity, and scientific rigor in all its activities. All parties with control over the content of IAS–USA activities are required to disclose to the organization and activity audience any financial interest or other relationship with the manufacturer(s) of any commercial product(s) or provider(s) of commercial services with interests discussed in the activity (eg, presentation, article, etc) within at least the past 12 months. Financial interests or other relationships

can include receipt of grants or research support, status as employee or consultant, stock or options holder, paid lecturer, paid lecturer, writer, or author, or member of speakers bureau, of the party or of his or her spouse or partner. The ACCME defines a financial interest as an interest of any dollar amount. Part of the IAS–USA policies to ensure the integrity of its activities is the policy to separate commercial promotion from core IAS–USA educational and informational activities. Individuals who conduct marketing or promotional activities for commercial firms may not contribute to core IAS–USA programs. A marketing or promotional activity includes any activity in which the commercial entity controls key elements, such as speaker or topic selection, that could be used to serve the entity’s commercial interests (eg, speakers bureaus, advertorials, etc). Individuals may not participate in most IAS–USA programs for 12 months after functioning in a promotional or marketing effort for a commercial firm. A notable exception to the separation policy is the annual Conference on Retroviruses and Opportunistic Infections (CROI) which allows research and symposia presentations by individuals with some of such relationships (including employment) because of its large focus on the presentations on original research, if their research or work passes rigorous peer review). Panel members who meet general criteria and are appointed, agree not to participate in any promotional activity on behalf of a pharmaceutical or medical device company (eg, serve on a speaker bureau, as a paid lecturer, or a similar contribution) while a member of the panel. Any conforming financial relationships with commercial entities that still may represent a real or potential COIs, will be resolved so that they do not influence the content of the recommendations. Prior to selection of the section teams and leaders, panel members declared their financial relationships with commercial concerns, discussed potential COIs, and recused themselves from serving as section leaders or team members accordingly.

### **III. The IAS–USA Antiretroviral Recommendations Panel**

The members of the IAS–USA Antiretroviral Recommendations Panel are listed in **eBox 2**. The Panel convened in person in October 2017 to April 2018, and regularly by conference call. The chair oversees the discussions of the process and evidence review and manuscript development, and guides the group to consensus. Section leaders and teams were appointed to evaluate evidence and summarize panel discussions for each section.

### **IV. Rating the Recommendations**

The Panel is divided by topic into working sections, each with a section leader. These sections are responsible for reviewing and screening evidence, developing preliminary recommendations, and presenting these to the full Panel for discussion, identification of further evidence, and consensus.

The selected rating system (**Manuscript Table 1**) combines 2 ratings for each recommendation. One rates the strength of the recommendation (strong, moderate, or limited support) and the other rates the quality of the evidence (ranging from Ia, based on evidence from 1 or more randomized controlled clinical trial[s] published in the peer-reviewed literature, to III, based on the Panel’s analysis of the accumulated available evidence).<sup>21</sup>

### **V. Content of the Recommendations**

The Panel agreed on the purpose, audience, and scope of these recommendations and on 8 main content sections (and subsections).

Content Sections:

1. When to Start
2. Recommended Initial Regimes
3. When and How to Switch
4. Laboratory Monitoring
5. Engagement and ART Adherence in the Context of 90-90-90
6. Cost
7. Prevention
8. Future Directions

Panel members were assigned to content sections based on their expertise and section leaders were appointed (**eBox 3**). The Panel Chair participates in all sections and reviews the entire manuscript, and Paul A. Volberding, MD, reviewed literature search results and identified relevant publications, and also reviewed the entire manuscript.

From October 2017 to June 2018, sections met in person and by conference call and e-mail exchange. Initial discussions were used to develop detailed Section outlines, and assign participants to draft subsections. The full Panel reviewed sections and the final manuscript.

## VI. Evidence Collection and Literature Searches

Panel members were selected based on their active work in the field of HIV research and care, and detailed knowledge of available evidence (published and presented at major scientific conferences).

Literature searches in PubMed and Embase were conducted and designed by an expert in systematic reviews, Hacsí Horvath and one of the panel members, Paul Volberding (**eTable 1**). The initial literature search provided data available since the 2016 publication of the recommendations through February 2018; approximately 237 references were ultimately identified. Relevant abstracts publically presented at recent scientific conferences were identified by panel members. All manufacturers of FDA-approved antiretroviral drugs were asked to submit lists of publications or abstracts meeting the established criteria (**eTable 2**). Drug manufacturers were instructed to provide references and electronic copies of the published or presented papers or abstracts only and not to comment on the design, methods, results or implications of any of the work. All reference lists, published papers, abstracts, and other relevant reports were organized and stored on a web-based, shared, electronic drive to which all panel members have ongoing access.

## eREFERENCES

1. Carpenter CCJ, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1996: recommendations of an international panel. *JAMA*. 1996;276(2):146-154. Ref ID: 795
2. Gunthard HF, Aberg JA, Eron JJ, et al. Antiretroviral treatment of adult HIV infection: 2014 recommendations of the International Antiviral Society-USA panel. *JAMA*. 2014;312(4):410-425. Ref ID: 13436
3. Günthard HF, Saag MS, Benson CA, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2016 recommendations of the International Antiviral Society-USA panel. *JAMA*. 2016;316(2):191-210. Ref ID: 14475
4. Carpenter CCJ, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1997: updated recommendations of the International AIDS Society–USA panel. *JAMA*. 1997;277:1962-1969. Ref ID: 989
5. Carpenter CCJ, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1998: updated recommendations of the International AIDS Society–USA panel. *JAMA*. 1998;280:78-86. Ref ID: 1382
6. Carpenter CCJ, Cooper DA, Fischl MA, et al. Antiretroviral therapy for HIV infection in adults: updated recommendations of the International AIDS Society–USA panel. *JAMA*. 2000;283(3):381-390. Ref ID: 1978
7. Hammer SM, Eron JJ, Jr., Reiss P, et al. Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. *JAMA*. 2008;300(5):555-570. Ref ID: 7755
8. Hammer SM, Saag MS, Schechter M, et al. Treatment for adult HIV infection: 2006 recommendations of the International AIDS Society-USA panel. *JAMA*. 2006;296:827-843. Ref ID: 6062
9. Thompson MA, Aberg JA, Cahn P, et al. Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society-USA panel. *JAMA*. 2010;304(3):321-333. Ref ID: 9521
10. Thompson MA, Aberg JA, Hoy JF, et al. Antiretroviral treatment of adult HIV infection: 2012 recommendations of the International Antiviral Society-USA panel. *JAMA*. 2012;308(4):387-402. Ref ID: 11418

11. Yeni PG, Hammer SM, Carpenter CCJ, et al. Antiretroviral treatment for adult HIV-1 infection in 2002: updated recommendations of the International AIDS Society-USA panel. *JAMA*. 2002;288:222-235. Ref ID: 4066
12. Yeni PG, Hammer SM, Hirsch MS, et al. Treatment for adult HIV infection: 2004 recommendations of the International AIDS Society-USA panel. *JAMA*. 2004;292:251-265. Ref ID: 5128
13. Hirsch MS, Conway B, D'Aquila RT, et al. Antiretroviral drug resistance testing in adults with HIV infection: implications for clinical management. International AIDS Society-USA Panel. *JAMA*. 1998;279(24):1984-1991. Ref ID: 1304
14. Hirsch MS, Brun-Vézinet F, D'Aquila RT, et al. Antiretroviral drug resistance testing in adult HIV-1 infection: recommendations of an International AIDS Society-USA Panel. *JAMA*. 2000;283(18):2417-2426. Ref ID: 2244
15. Hirsch MS, Brun-Vézinet F, Clotet B, et al. Antiretroviral drug resistance testing in adults infected with human immunodeficiency virus type I: 2003 recommendations of an International AIDS Society-USA panel. *Clin Infect Dis*. 2003;37:113-128. Ref ID: 4617
16. Hirsch MS, Günthard HF, Schapiro JM, et al. Antiretroviral drug resistance testing in adult HIV-1 infection: 2008 recommendations of an International AIDS Society-USA panel. *Clin Infect Dis*. 2008;47(2):266-285. Ref ID: 7276
17. Schambelan M, Benson CA, Carr A, et al. Management of metabolic complications associated with antiretroviral therapy for HIV-1 infection: recommendations of an International AIDS Society-USA panel. *JAIDS*. 2002;31(3):257-275. Ref ID: 3494
18. Whitley RJ, Jacobson MA, Friedberg DN, et al. Guidelines for the treatment of cytomegalovirus diseases in patients with AIDS in the era of potent antiretroviral therapy. *Arch Intern Med*. 1998;158:957-969. Ref ID: 1393
19. Saag MS, Holodniy M, Kuritzkes DR, et al. HIV viral load markers in clinical practice. *Nat Med*. 1996;2(6):625-629. Ref ID: 836
20. Martin DF, Dunn JP, Davis JL, et al. Use of the ganciclovir implant for the treatment of cytomegalovirus retinitis in the era of potent antiretroviral therapy: recommendations of the International AIDS Society-USA panel. *Am J Ophthalmol*. 1999;127(3):329-339. Ref ID: 2330
21. Canadian Task Force on the Periodic Health Examination. The periodic health examination. *Can Med Assoc J*. 1979;121(9):1193-1254. Ref ID: 11289

## eBox 1. Volunteer IAS–USA Board of Directors, January 2018

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Professor of Medicine  
Co-Director, Center for AIDS Research  
Director, AIDS Research Institute  
University of California San Francisco  
San Francisco, California

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Professor of Medicine  
I.D. Training Program Director  
Director, Antiviral Research Center (AVRC)  
PI/Director, HIV/AIDS Clinical Trials Unit  
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Chief, Division of Infectious Disease  
Associate Director, Clinical AIDS  
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Professor of Medicine  
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Rollins School of Public Health  
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Robert Schooley, MD  
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Head, Division of Infectious Diseases  
Vice Chair, Department of Medicine  
Senior Director, International Initiatives  
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La Jolla, California

## eBox 2. IAS–USA Antiretroviral Therapy Recommendations Panel

Michael Saag, MD (Panel Chair)\*  
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Jim Straley Chair in AIDS Research  
Director, Center for AIDS Research  
Associate Dean for Global Health, School of  
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University of Alabama at Birmingham  
Birmingham, Alabama

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ID Training Program Director  
Director, Antiviral Research Center (AVRC)  
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Bridge HIV|Population Health Division|San  
Francisco Department of Public Health  
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Hubert Professor and Chair Department of  
Global Health  
Professor of Medicine  
Emory University School of Medicine  
Rollins School of Public Health  
Atlanta, Georgia

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Harvard Medical School  
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President of the Swiss HIV Cohort Study  
Deputy Chief, Division of Infectious Diseases  
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Associate Director  
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Director, UAB CFAR Clinical Core  
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Director, AIDS Research Institute  
University of California San Francisco  
San Francisco, California

\*IAS–USA Board of Directors liaison

## **eBox 3. Working Sections of the IAS–USA Antiretroviral Therapy Recommendations Panel**

- **When to Start**  
Section Team: Melanie A. Thompson, MD (Leader), Constance A. Benson, MD, Jennifer H. Hoy, MBBS, Raphael J. Landovitz, MD, Jean-Michel Molina, MD, PhD, and Paul A. Volberding, MD
- **Recommended Initial Regimens**  
Section Team: Rajesh T. Gandhi, MD (Leader), Constance A. Benson, MD, Joseph J. Eron, Jr, MD, Gerd Fätkenheuer, MD, Huldrych F. Günthard, MD, Jean-Michel Molina, MD, PhD, and Paul A. Sax, MD
- **When and How to Switch**  
Section Team: Jennifer F. Hoy, MBBS (Leader), Carlos del Rio, MD, Joseph J. Eron, Jr, MD, Gerd Fätkenheuer, MD, and Rajesh T. Gandhi, MD
- **Laboratory Monitoring**  
Section Team: Davey M. Smith, MD (Leader), Huldrych F. Günthard, MD, Jennifer H. Hoy, MBBS, Michael J. Mugavero, MD, MHSc, and Melanie A. Thompson, MD
- **Engagement and ART Adherence in the Context of 90-90-90**  
Section Team: Michael J. Mugavero, MD, MHSc (Leader), Susan P. Buchbinder, MD, Carlos del Rio, MD, Joseph J. Eron, Jr, MD, Davey M. Smith, MD, and Melanie A. Thompson, MD
- **Cost**  
Section Team: Paul E. Sax, MD (Leader), Gerd Fätkenheuer, MD, Huldrych F. Günthard, MD, Michael J. Mugavero, MD, MHSc, and Davey M. Smith, MD
- **Prevention**  
Section Team: Raphael J. Landovitz, MD (Leader), Constance A. Benson, MD, Susan P. Buchbinder, MD, Michael J. Mugavero, MD, MHSc
- **Future Directions**  
Section Team: Constance A. Benson, MD (Leader), Susan P. Buchbinder, MD, Rajesh T. Gandhi, MD, Raphael J. Landovitz, MD, Jean-Michel Molina, MD, PhD, Paul A. Sax, MD, and Paul A. Volberding, MD

**eTable 1. Summary of Evidence Collection**

Evidence Identification	Number of References From the Initial Search	Number of References Considered Possibly Relevant (Ultimately)
<b>April 2018 Submission</b>		
Relevant published reports and meeting abstracts <ul style="list-style-type: none"> <li>• PubMed and EMBASE searches (05/31/2016 to 02/01/2018)</li> </ul>	<b>&gt;4490</b>	<b>237</b>
<ul style="list-style-type: none"> <li>• Panel members' identification*</li> </ul>	ongoing	
Number of relevant references reported in manuscript (submitted <b>April 2018</b> )		<b>164</b>

\*Of note, individual panel members collected relevant evidence throughout the process and reviewed materials submitted by manufacturers (particularly for safety issues) and this process cannot be quantified.

**eTable 2. Search Terms Used and Results of Embase and PubMed Literature Searches\***

**MONTHLY SEARCH STRATEGY**

Search	EMBASE QUERY	Results
#16	Search #1	167
#15	Search #1	155
#14	Search #1	156
#13	Search #1	161
#12	Search #1	189
#11	Search #1	220
#10	Search #1	192
#9	Search #1	143
#8	Search #1	150
#7	Search #1	179
#6	Search #1	195
#5	Search #1	172
#4	Search #1	210
#3	Search #1	163
#2	Search #1	189
#1	<p>(((("HIV Infections"[Majr] AND "Anti-Retroviral Agents"[Mesh] AND ((Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb]) AND hasabstract[text] AND ("2012/07/01"[PDat] : "3000/12/31"[PDat]) AND English[lang] AND adult[MeSH]))) OR (((HIV AND antiretroviral*) NOT medline[sb] AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])) AND hasabstract[text] AND ("2012/07/01"[PDat] : "3000/12/31"[PDat]))) OR (HIV Infections[majr] AND Anti-Retroviral Agents[mh] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR MetaAnalysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb]) AND ("2012/07/01"[PDat] : "3000/12/31"[PDat]) AND English[lang] NOT (child[mh] OR pediatr*[ti] OR paediatr*[ti] OR adolescen*[ti] OR child*[ti] OR infan*[ti] OR neonat*[ti] OR newborn*[ti] NOT (adult[mh] OR adult*[ti]))) OR (HIV Infections/dt[majr] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled</p>	201

	<p>Clinical Trial [ptyp] OR  Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp]  OR systematic[sb]) AND  ("2012/07/01"[PDat] : "3000/12/31"[PDat]) AND English[lang] NOT (child[mh] OR  pediatr*[ti] OR paediatr*[ti] OR  adolescen*[ti] OR child'[ti] OR infan*[ti] OR neonat*[ti] OR newborn*[ti] NOT (adult[mh]  OR adult'[ti])) OR (HIV  Infections[majr] AND Antiretroviral Therapy, Highly Active[mh] AND (Clinical Trial[ptyp]  OR Comparative  Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter  Study[ptyp] OR Randomized  Controlled Trial [ptyp] OR systematic[sb]) AND ("2012/07/01"[PDat] :  "3000/12/31"[PDat]) AND English[lang] NOT  (child[mh] OR pediatr*[ti] OR paediatr'[ti] OR adolescen*[ti] OR child'[ti] OR infan*[ti]  OR neonat*[ti] OR  newborn*[ti] NOT (adult[mh] OR adult*[ti]))) NOT letter[pt]</p>	
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Search	PUBMED QUERY	Results
#20	Search #1	146
#19	Search #1	94
#18	Search #1	106
#17	Search #1	101
#16	Search #1	124
#15	Search #1	118
#14	Search #1	76
#13	Search #1	77
#12	Search #1	57
#11	Search #1	60
#10	Search #1	40
#9	Search #1	111
#8	Search #1	47
#7	Search #1	86
#6	Search #1	70
#5	Search #1	63
#4	Search #1	109
#3	Search #1	109
#2	Search #1	96
#1	(((("HIV Infections"[Majr]) AND "Anti-Retroviral Agents"[Mesh] AND ((Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled. Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter	71

<p>Study[ptyp] OR Randomized  Controlled Trial[ptyp] OR systematic[sb]) AND hasabstract[text] AND  ("2012/07/01"[PDat] : "3000/12/31"[PDat])  AND English[lang] AND adult[MeSH])) OR (((HIV AND antiretroviral*) NOT  medline[sb] AND  ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR  clinical trial[Publication Type]  OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic  use[MeSH Subheading])) AND  hasabstract[text] AND ("2012/07/01"[PDat] : "3000/12/31"[PDat])) OR (HIV  Infections[majr] AND Anti-Retroviral  Agents[mh] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled  Clinical Trial[ptyp] OR MetaAnalysis[  pty/l] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR  systematic[sb]) AND  ("2012/07/01"[PDat] : "3000/12/31"[PDat]) AND English[lang] NOT (child[mh] OR  pediatr*[ti] OR paediatr*[ti] OR  adolescen*[ti] OR child*[ti] OR infan*[ti] OR neonat*[ti] OR newborn*[ti] NOT (adult[mh]  OR adult*[ti])))) OR (HIV  Infections/dt[majr] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled  Clinical Trial [ptyp] OR  Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp]  OR systematic[sb]) AND  ("2012/07/01"[PDat] : "3000/12/31"[PDat]) AND English[lang] NOT (child[mh] OR  pediatr*[ti] OR paediatr*[ti] OR  adolescen*[ti] OR child'[ti] OR infan*[ti] OR neonat*[ti] OR newborn*[ti] NOT (adult[mh]  OR adult'[ti])))) OR (HIV  Infections[majr] AND Antiretroviral Therapy, Highly Active[mh] AND (Clinical Trial[ptyp]  OR Comparative  Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter  Study[ptyp] OR Randomized  Controlled Trial [ptyp] OR systematic[sb]) AND ("2012/07/01"[PDat] :  "3000/12/31"[PDat]) AND English[lang] NOT  (child[mh] OR pediatr*[ti] OR paediatr'[ti] OR adolescen*[ti] OR child'[ti] OR infan*[ti]  OR neonat*[ti] OR  newborn*[ti] NOT (adult[mh] OR adult*[ti])))) NOT letter[pt]</p>	
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- **Pooling Embase and PubMed results for 05/31/2016 through February 2018 (including “ahead of print” records): 4494**

**eTable 3. Information Requested From Antiretroviral Drug Manufacturers**

Manufacturer	Information Requested	Date Requested	Date Received
AbbVie	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>	09/29/2017	12/22/2017
Boehringer Ingelheim Pharmaceuticals, Inc	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> <li>•</li> </ul>	09/29/18	<b>N/A</b>
Bristol-Myers Squibb	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>	09/29/2017	<b>N/A</b>
Genentech	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>	09/29/2017	<b>N/A</b>
Gilead Sciences, Inc	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> </ul>	09/29/2017	12/04/2017

	<ul style="list-style-type: none"> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>		
Janssen Therapeutics	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>	09/29/2017	01/03/2018
Merck & Co, Inc	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>	09/29/2017	01/02/2018
Theratechnologies	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>	12/13/2017	01/04/2018
ViiV Healthcare	<ul style="list-style-type: none"> <li>• Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>• Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>• Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>	09/29/2017	12/15/2017