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HIV pipeline-lite 2020

New drugs in development

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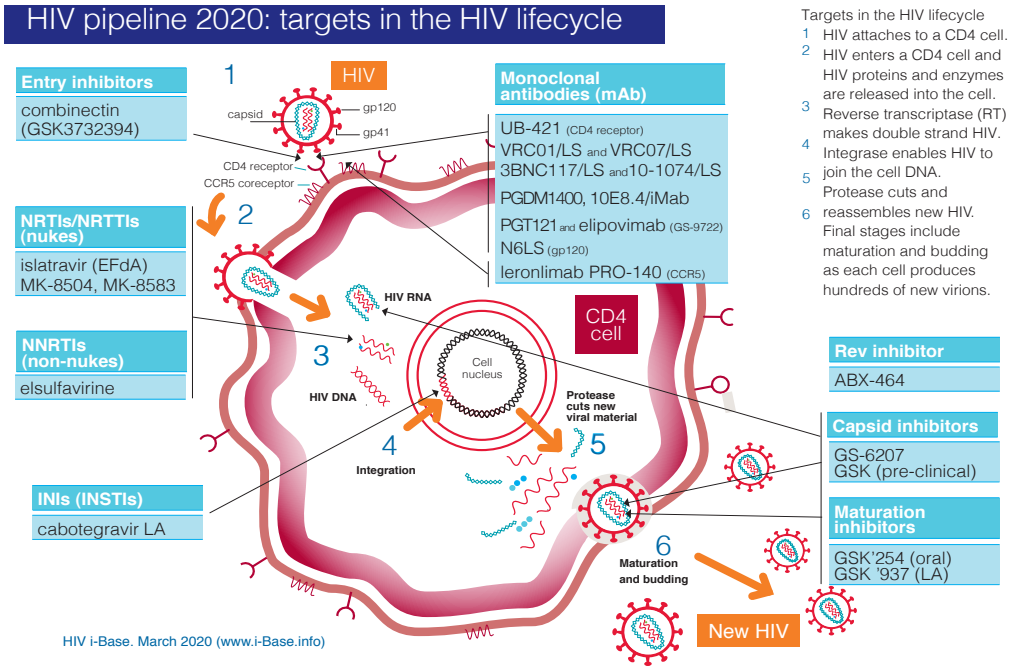

Figures and tables

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HIV pipeline 2020 update: new drugs in development

Simon Collins, HIV i-Base

This is the fourth year that i-Base has produced the HIV pipeline review as part of our Fit for Purpose report on antiretroviral treatment optimisation.

Two versions are available:

1. The full version includes more information for each drug, with full references.
2. This "Pipeline-lite" version has a summary for each drug and is included in the i-Base Fit For Purpose report.

Both electronic versions (web and PDF) include hyperlinks to all research sources and references.

This review is based on HTB reports over the last eight months and coverage from CROI, IAS, EACS and other conferences.

http://www.i-Base.info/hiv-pipeline-report-2020

h-tb

HIV TREATMENT BULLETIN

Editor: Simon Collins
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HTB is a not-for-profit community publication that aims to provide a review of the most important medical advances related to clinical management of HIV and its related conditions as well as access to treatments. Comments to articles are compiled from consultant, author and editorial responses.

HIV i-Base is a registered charity no 1081905 and company reg no 3962064. HTB was formerly known as DrFax.

Introduction: eight months since IAS 2019

This report is based on new developments over the last eight months since the pipeline report produced for the IAS conference in July 2019. [1]

This includes the move towards simplified ART and long-acting compounds in several drug classes that allows less frequent dosing than daily oral ARVs.

It also includes using bNAbs as a rescue treatment for people with multiclass HIV resistance. So while ibalizumab has already been approved with an orphan-drug designation for multidrug resistance, this potential is shared with dozens of other bNAbs and other new classes including long-acting capsid inhibitors.

It is notable that the companies developing new drugs for treatment and prevention are also investing in HIV cure.

The report also includes references to 30 studies at CROI 2020 that cover a wide range of pipeline compounds. They include islatravir, MK-8504 and 8583, bNAbs (including VRC01, PGT-121, GS-9722, 3BNC117, 10-1074, N6-LS), GS-6207 (capsid inhibitor), GSK3640254 (maturation inhibitor), elsulfavirine, combinectin, ABX464, BIT255 and GS-9131.

Regulatory approvals and submissions (Table 1)

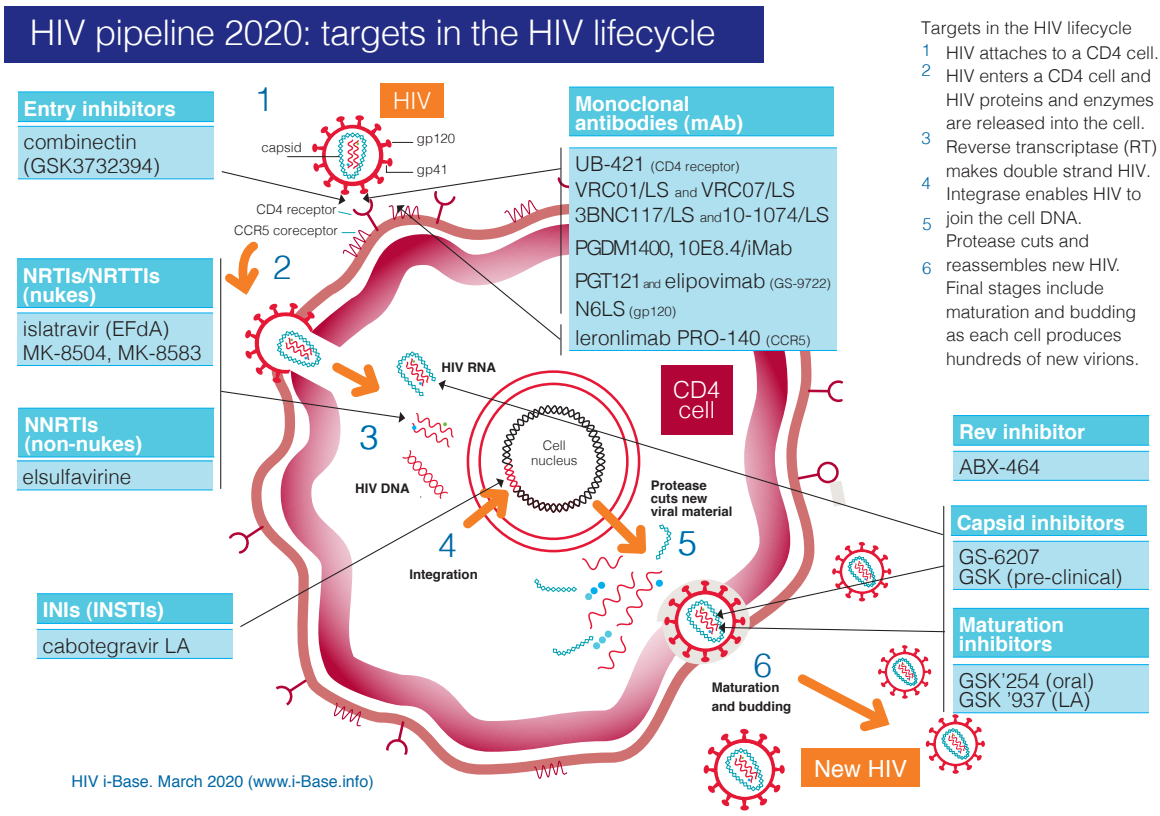
Recent approvals include the HIV monoclonal antibody ibalizumab (Trogarzo) in the EU (18 months after approval in the US). [2, 3] See Table 1.

The gp-120 attachment inhibitor fostemsavir was submitted to the FDA in December 2019 and to the EMA in January 2020 based on 96-week results from the BRIGHTE study. [4, 5, 6]

However, the regulatory application for the long-acting injections of cabotegravir LA and rilpivirine LA (Cabenuva) was not approved by the FDA within the fast-track timeline. [7] This was unexpected given good results from the phase 3 FLAIR and ATLAS studies. [8] The was due to manufacturing problems from scaling up to industrial production and there are no safety and efficacy concerns. Ongoing studies are already looking at practical issues of using these injectable drugs. [9, 10, 11]

ViiV has also submitted a new application to the FDA for a switch indication for the dual combination of dolutegravir/lamivudine (Dovato), based on 48-week results from the phase 3 TANGO study, presented at IAS 2019. [12, 13]

Figure 1: HIV pipeline 2020: targets in the HIV lifecycle



Key: INSTI: integrase strand transfer inhibitor; LA: long-acting; mAb: monoclonal antibody; NRTI: nucleoside/tide reverse transcriptase inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor.

Dolutegravir/lamivudine was approved in the EU as first-line ART in July 2019 [14] and extended follow-up to 96-weeks for the GEMINI 1 and 2 studies in treatment naive participants were presented at IAS 2019. [15]

Updates from CROI 2020 include looking at the importance of other background drugs with ibalizubmab. [82] It also includes results from the ATLAS-2M study reporting that cabotegravir/ rilpivirine LA injections can be used every two months. [83]

About a dozen posters look at dual ART, largely dolutegravir/ lamivudine, including updates from the phase 3 GEMINI and TANGO studies. [84, 85, 86]

Compounds in development by class

Integrase inhibitors

cabotegravir LA

The 2019 pipeline report summarised the clinical efficacy and safety of long-acting cabotegravir and rilpivirine injections and the regulatory complications are discussed above. [1]

However, the US National Institute for Allergy and Infectious Diseases (NIAID) recently announced a new study using cabotegravir LA (without rilpivirine) in a dual combination with VRC07-523LS - a long-acting bNAb. [16, 17]

ViiV also recently announced an agreement to develop another bNAb developed by NIAID called N6LS (see later below). [18]

Cabotegravir is also being developed as a 6-monthly PrEP implant.

NRTIs

islatravir (EFdA)

Islatravir is an NRTI in development by Merck that is notable for very high potency, a long plasma half-life (~120 hours) that allows weekly and perhaps monthly oral dosing and a slow-release removable implant that might only require annual dosing.

Ongoing studies are for use as both treatment and PrEP. It is classified as a nucleoside reverse transcriptase translocation inhibitor (NRTTI) and has multiple mechanisms of action. [19]

Table 1: Recent regulatory approvals and submissions

Compound/formulation	Class	Approved / submitted	Company
ibalizumab	bNAb.	Approved US: April 2018. Approved EU: Sep 2018.	Theratechnologies
fostemsavir	gp120 attachment inhibitor.	Submitted US: Dec 2019. Submitted EU: Jan 2020.	ViiV Healthcare
cabotegravir LA and rilpivirine LA injections	INSTI + NNRTI injections.	Submitted US: Apr 2019 Submitted EU: July 2019	ViiV Healthcare Janssen
cabotegravir oral	INSTI - oral formulation used for lead-in dosing.	Submitted US: Apr 2019 Submitted EU: July 2019	ViiV Healthcare Janssen
elsulfavirine, prodrug of VM-1500A	NNRTI - similar activity to efavirenz. Long-acting monthly IM/SC injections. 96-week phase 2 results at AIDS 2018.	Apparently licensed in Russia. No published phase 3 data or submission to FDA or EMA.	Viriom

Table 2: HIV pipeline compounds by development phase (excluding individual bNAbs)

Compound/Company	Class	Notes	Phase
islatravir (EFdA) Merck/MSD	NRTTI	Highly potent, low dose, active against NRTI resistance. Long half-life, potential as oral (dosed daily, weekly and perhaps monthly) and an implant (annual). Monthly and annual formulations are for PrEP.	Phase 2/3
islatravir / 3TC / doravirine Merck/MSD	FDC: NRTTI + NRTI + NNRTI	FDC with generic 3TC and NNRTI doravirine. Current studies used triple combination for initial ART and switch to islatravir/doravirine for dual maintenance ART.	Phase 3
islatravir/ doravirine Merck/MSD	FDC: NRTTI + NNRTI	Dual FDC with NNRTI doravirine. Currently studies look at a switch option after viral suppression with triple drug ART.	Phase 3
GSK3640254 GSK/ViiV Healthcare	maturation inhibitor	Maturation inhibitor acquired from BMS that has just entered phase 2 studies. Phase 1 results reported in May 2019.	Phase 2
GS-6207 Gilead	capsid inhibitor	Early stage for new class with activity at multiple stages of viral lifecycle. Sub-cutaneous injection every six months. Phase 1 data presented at IAS 2019 and in press release in November 2019.	Phase 2
elsulfavirine (VM-1500)	NNRTI	Developed by Viriom, already used in Russia as once daily oral drug. Long-acting formulation in develpoment for monthly IM or SC injection.	Phase 2
MK-8504 and MK-8583	NRTI	Tenofovir prodrugs from Merck, both with completed phase 1 studies.	Phase 1
Combinectin (GSK3732394) ViiV Healthcare	entry inhibitor gp41 and CD4	Combined adnectin/fusion inhibitor that stops viral entry by targeting multiple sites of action and the potential for self-administered once-weekly injections.	Phase 1
bNAbs: leronlimab, UB-421, VRC01, 3BNC117, 10-1074,10E8, N6, PGDM1400 and PGT121 etc.	bNAb's: Multiple targets include CD4 binding, v3 loop etc	Many bNAbs are in development for prevention, treatment and cure research - often in long-acting LS formulations and in dual or triple combinations. Many public and private research institutes (NIH, Rockefeller etc) and pharmaceutical research companies (Gilead, ViiV etc). See Table 3.	Preclincal, Phase 1 to 3

New results on islatravir both as treatment and PrEP were presented at IAS 2019.

A phase 2b dose-ranging study led to selecting the 0.75 mg daily dose. It also provided first data on dual therapy with islatravir and doravirine. [20, 21]

Phase 3 studies using a two-drug fixed dose combination of doravirine/islatravir are already planned or ongoing. [22, 23, 24]

Details on once-weekly oral dosing dual ART, with another long-acting compound in pre-clinical development have not been announced (but see MK-8504 and MK-8683 below).

Islatravir PrEP studies include an ongoing phase 2 study using an oral formulation for once-monthly dosing. [25] If this is effective, it will have the potential to significantly expand the indication for PrEP from a relatively small group of people at high risk of HIV to the billions of people globally who are sexually active but whose HIV risk is much smaller.

IAS 2019 included results on an islatravir implant for PrEP (now at the 62 kg dose). [26]

Updates from CROI 2020 include a late breaking oral presentation on PrEP efficacy in a macaque study using weekly oral islatravir and two posters related to metabolic outcome and dose selection. [87, 88, 89]

MK-8504 and MK-8583

There are few details on the other long-acting compounds Merck plans to study islatravir with but MK-8504 and MK-8583 are two tenofovir prodrugs studies in HIV positive phase 1 studies.

A single dose of MK-8504 (100 mg or 240 mg) produced reductions in viral load of about –1.0 log (range +0.5 to –1.5) copies/mL. [27]

Results have not yet been published for MK-8583. [28]

Updates from CROI 2020 include a poster on these two compounds reporting on antiviral efficacy from single doses. [90]

GSK NRTTI

GSK have also filed several patents for NRTTI compounds that are currently pre-clinical stages with plans to formulate these as a long acting injection.

bNABs

A growing number of HIV broadly neutralising monoclonal antibodies (bNAbs) are now in development - with more to follow, engineered to improve potency, breadth of coverage and half-life etc.

They generally need to be used in combinations and also require sensitivity testing at baseline to know whether or not they are likely to be active. These sensitivity tests are also in early stage development.

Long-acting formulations - called LS from the two mutation changes - bring the potential of extended dosing schedules - from 2 to 6 months.

Drug resistance has so far reported for all individual bNAbs, and strategies to reduce this risk include use of combination bNAbs and engineering bispecific or trispecific compounds.

Although there have been few new clinical studies presenting new data since CROI 2019, several new studies have been launched and both ViiV and Gilead have announced licensing rights to develop some of the most promising bNAbs.

The number of studies referenced below for each of the most promising bNAbs show the research interest in this field but is unlikely to be comprehensive. An updated table of these and other compounds is produced by Richard Jefferys at TAG as part of a resource on cure-related trials. [29]

CROI 2020 includes several studies looking at bNAbs in general including baseline susceptibility, tissue penetration (including CSF). Several studies related to aspects of individual compounds in adults and infants, including leronlimab, VRC01, N6-LS and 3BNC117. [91, 92, 93, 94, 95, 96, 97, 98]

leronlimab (PRO140)

Leronlimab is a humanised IgG4 monoclonal antibody that blocks HIV entry by binding to CCR5 but is active against maraviroc-resistant virus.

This compound has been in development for more than a decade and is being studied both as part of ART and as monotherapy after viral suppression on oral ART.

Ongoing studies include a phase 2/3 study in 25 treatment-experienced participants. [30]

A much larger US phase 2b/3 study has enrolled more than 550 HIV positive participants on stable ART.[31, 32]

According to a more recent press release from August 2019, more than 150 participants have maintained undetectable viral load out to one year. The study completion date is listed as July 2020. [33]

Leronlimab is also being studied in non-HIV setting as prophylaxis against graft vs host disease (GVHD) in people undergoing allogeneic stem cell transplant. [34]

Leronlimab is being developed by CytoDyn.

CROI 2020 includes a poster on use in four-class resistance. [92]

Table 3: bNAbs for HIV prevention, treatment or cure research

Compound / Company	Target	Notes	Status
ibalizumab	gp120	Already approved in the US and EU for treatment of MDR HIV.	Approved.
leronlimab (PRO 140) CytoDyn	CCR5	Once-weekly sub-cutaneous injection being studied in addition to ART for multi-drug resistance and as monotherapy maintenance therapy (without ART). Phase 3.	Phase 3.
UB-421 United BioPharma	CD4 binding	Infusion dosed either weekly or every two weeks as alternative to ART during treatment interruption. Phase 3.	Phase 3.
VRC01 and VRC01LS US NIH	CD4 binding	Intravenous infusion being studied in cure research and as PrEP (2 large phase 3 studies are ongoing). Sub-cutaneous dosing of infants to prevent transmission at birth or from breastfeeding. VRC01LS is a longer acting formulation. Results as PrEP expected late 2020.	Phase 3.
VRC07, VR07-523LS	CD4 binding	Engineered from VRC01. Being studied with cabotegravir-LA in ACTG trial.	Phase 2.
PGT-121 and GS-9722 (elipovimab). Gilead.	C3/V3	PGT121 is an IgG1 mAb that targets the V3 Env epitope. GS-9722 (elipovimab) is engineered from PGT-121.	Phase 1.
3BNC117 and 10-1074; Rockefeller University and Gilead	CD4 binding and C3/V3	Both bNAbs are available as LS long-acting formulations. Gilead Sciences signed for exclusive global development rights.	Phase 2.
N6 US NIH and ViiV	gp120	Developed by US NIH and now licenced to ViiV.	Phase 1.
Other mAbs: 10E8, trispecific bNAbs, PGDM1400	MPER, V2 and others	Mulitple compounds in preclinical and phase 1 studies.	Phase 1.

UB-421

UB-421 is a broadly neutralising mAb that targets CD4 binding. In vitro data suggest comparable or greater potency compared to other compounds, including VRC01 and 3BNC117.

Results from a phase 2 study were published in the New England Journal of Medicine in April 2019. This used UB-421 monotherapy during an 8-week treatment interruption. UB-421 was given by infusion every two-weeks. [35]

Several studies are listed as expecting to start in 2020. Although the same studies have been listed since 2017 with the starting dates changing each year. [36, 37, 38] These include adding UB-421 to ART to reduce the HIV reservoir and a phase 3 switch study to UB-421 monotherapy.

UB-421 is being developed by United BioPharma with all sites in Taiwan.

No updates are expected at CROI 2020.

VRC01 and VRC01LS

VRC01 is an early broadly neutralising mAb (active against 80-90% HIV strains) that targets the CD4 binding site. It can be given by infusion or sub-cutaneous injection and has been studied in phase 1/2 development with multiple indications: for treatment, prevention and as a component of cure research.

Most ongoing studies are looking at VRC01 for HIV prevention, with two large international dose-finding, placebo-controlled phase 2 studies using VRC01 as PrEP. [39, 40]

Although results are expected in late 2020 there are concerns about using a single mAb given limited breadth and potency from one compound. [41]

VRC01 is being studied as part of a dual bNAb combination with 10-1074 in a phase 1 study in 75 HIV positive people on suppressed ART who will be asked to stop HIV treatment. [42]

A phase 1 study is looking at VRC01 with ART in 25 HIV positive people diagnosed during primary infection, with sites in Kenya, Tanzania and Thailand. [43]

The long-acting formulation - VRC01LS - is also in phase 1 studies. This includes using a single injection of VRC01LS in infants after birth to limit risk of vertical transmission and a potential role of additional injections for breastfed infants. [44, 45]

Another phase 1 study is looking at responses to VRC07 in eight people who received VRC01LS. [46]

CROI 2020 includes studies on VRC01 tissue penetration and use as infant prophylaxis. [93, 94, 95, 96]

VRC07 and VR07-523LS

VRC07 is an engineered clonal relative to VRC01 and includes VRC07-523LS which is a second-generation bNAb with improved potency, breadth, expression and an LS version to extend the half-life.

Results from a phase 1 safety study in 26 HIV negative participants was published in Lancet HIV in October 2019. [47]

It is now being studied alone and in combination with other bNAbs including 10E8VLS, PGT121 and PGDM140 in at least seven studies, usually phase 1 in HIV negative participants. However, this also includes a study in HIV-exposed infants and at least two studies in HIV positive adults. [45, 48, 49]

A new ACTG study (ACTG 5837) was announced that uses cabotegravir-LA every 4 weeks with VRC07-523LS every two months. [50]

NIAID have also granted TaiMed a non-exclusive license to develop VRC07-523LS in combination with the company's other bNAbs. [51]

No updates are expected at CROI 2020.

PGT-121 and GS-9722 (elipovimab)

PGT121 is an IgG1 mAb that targets the V3 Env epitope. Results of a randomised double blinded, dose escalation, placebo-controlled trial phase 1 study were presented at CROI 2019. [52]

Results in 15 treatment-naive participants, reported that a single infusion of PGT121 produced a median viral load reduction of –1.7 log copies/mL in participants with high baseline viral load, but breakthrough with bNAb resistance also occurred quickly when used as monotherapy.

Two phase 1 studies in HIV negative participants are ongoing but a third phase1/2 study with other bNAbs includes HIV positive participants. [49]

PGT-121 was licensed from IAVI/Theraclone to Gilead in 2014 who developed a derivative called elipovimab (GS-9722), which was also reported at CROI 2019. [53] No ongoing or planned studies are currently listed for elipovimab.

Studies at CROI 2020 include new animal data on PGT-121 and looking at the viral reservoir and viral rebound and results from a phase 1 PK study of GS-9722 in HIV positive people. [99, 100, 101, 102]

3BNC117, 10-1074 and LS formulations

3BNC117 targets the CD4 binding site and 10-1074 targets the base of the V3 loop of the HIV envelope protein so in combination there is no cross resistance.

Both bNAbs were developed at Rockefeller University. When used together, a study reported at CROI 2019 reported that 2/13 participants maintained viral load below detection for over a year after interrupting ART, with one person extending this to two years. [54]

Both bNAbs are now engineered into long-acting LS formulations that might enable 6-monthly infusions. It is significant that in January 2020, Gilead announced it had signed licensing agreement for both exclusive and global development rights. [55, 56]

Several phase 1 studies are already ongoing using this combination in HIV positive participants, two of which include treatment interruptions. [57, 58, 59, 60]

A UK placebo-controlled study is also using both long-acting bNAbs to maintain viral suppression during a treatment interruption. The RIO study plans to enroll 75 HIV positive people who were diagnosed during primary infection and who started immediate ART. [61]

A phase 2 study uses 3BNC117 in combination with the fusion inhibitor albuvirtide (approved in China as a one-weekly formulation, similar to enfuvirtide) as maintenance therapy in 80 HIV positive participants on stable ART, in US sites. [62]

Studies at CROI 2020 on 3BNC117 include a reservoir study with romidepsin and on 10-1074 include a PK study on infant prophylaxis. [98, 94]

N6 and N6-LS

N6 is a bNAb also developed by the US NIH from the VRC01 class, engineered to have higher potency, active against 98% of isolates tested and also developed into a long-acting LS formulation. [63]

The only study currently listed is an ongoing phase 1 study in 40 HIV negative participants. [64]

In November 2019, ViiV Healthcare announced that it had negotiated an exclusive license to develop N6LS for both treatment and prevention of HIV. [65]

Studies at CROI 2020 include a phase 1 dose escalation study in HIV negative people, a CNS immune activation study in macaques and another looking at dynamics of viral rebound with TLR-7 agonist GS-9620. [97, 99, 100]

Other bNAbs: 10E8, trispecific bNAbs, PGDM1400

Several other promising antibodies are in development.

10E8v2.0/iMab is a bispecific antibody that showed almost 100% neutralisation breadth across a 118-member pseudotyped panel with mean inhibitory concentration of 0.002 ug/mL. It has also prevented infection in mouse studies. [66]

A phase 1 dose escalation study using both IV and subcutaneous formulations includes HIV positive people not yet on ART (as well as HIV negative participants). [67]

However, while the safety and tolerability of bNAbs are generally good, one study using 10E8 was recently put on hold due to grade 3 skin erythema in 7/8 participants. [68]

Preliminary results for a trispecific bNAb were presented at CROI 2019. This is the result of a joint development by the Vaccine Research Centre at NIAID and Sanofi where a single molecule could interact with three independent envelope regions: the CD4 binding site, MPER and the V1V2 glycan site. [69]

PGDM1400-1412 is a range of bNAbs with high potency and PGDM 1400 is already included in two recruited ongoing phase 1 studies including HIV positive people in combinations with PGT-121, VRC07-523LS and 10-1074. [70, 71]

A phase 1/2a study is also ongoing in HIV positive people in combination with PGT121, VRC07-523LS and PGDM1400. [49]

Capsid inhibitors

GS-6207

Capsid is the cone-shaped structural core within the HIV virion that protects HIV RNA and related enzymes. The capsid inhibitors are active in both early and later stages of the HIV lifecycle.

Phase 1 results with GS-6207 at IAS 2019 reported mean –2.2 log reduction at day 10 with GS-6207 monotherapy in treatment-naive participants (at which point ART was started). [72]

Further phase 1 results at EACS 2019 supported development of a modified six-monthly sub-cutaneous injection. [73]

A phase 2 study in 175 treatment naive participants will use oral GS-6207 to cover the first two weeks before using subcutaneous infusion of the capsid inhibitors, with oral F/TAF used throughout. However, when the infusion is repeated after six months, background F/TAF will be switched to dual ART with either daily oral TAF or daily oral bictegravir. [74]

A second study, also currently enrolling in US sites is a phase 2/3 study to GS-6207 with optimised ART in 100 treatment experienced people with multidrug resistance. A second cohort will run for people who don't meet criteria for initial randomisation, or for when this study is fully enrolled. [75]

Studies at CROI 2020 include an oral presentation and posters on antiviral activity and PK and another poster on resistance, [103, 104, 105, 106]

Maturation inhibitors

GSK3640254

The maturation inhibitor GSK3640254 works at the late stage of the viral lifecycle, by producing non-infectious, undeveloped HIV.

Results from two phase 1 studies in HIV negative adults that reported good safety outcomes and bioavailability of two different formulations were presented last year. [76] These supported further development as a once-daily oral pill.

A proof of concept, phase 2 dose-finding study is ongoing in 34 treatment-naive HIV positive participants. [77]

GSK '937 is a second maturation inhibitor compound in preclinical development as a long acting injectable formulation (both subcuteaous and intramuscular). Both compounds are being developed by GSK/ViiV.

Studies at CROI 2020 include a poster on preclinical development of second generation maturation inhibitors. [107]

Other compounds

Although little data has been reported for the following compounds over the last year (at least), they are still in active development.

Elsulfavirine (VM-1500A)

Elsulfavirine (a prodrug of VM-1500A) is an NNRTI being developed by Viriom that is currently being used in Russia. [78]

A long-acting injectable formulation is in development, with results from an animal study presented at IAS 2017, showing the potential for monthly by intramuscular (IM) or subcutaneous (SC) injection. [79]

CROI 2020 includes the first safety and PK results for the long-acting formulation of elsulfavirine. [108]

Combinectin (GSK3732394)

Combinectin (GSK3732394) is a biologic combined adnectin/fusion inhibitor that stops viral entry by targeting multiple sites of action on gp41 and CD4. This compound has the potential for self-administered once-monthly subcutaneous injections.

A summary of in vitro activity and resistance data and virologic data from mouse studies were presented at Glasgow 2016. [80]

In June 2019 the first phase 1 study in HIV negative volunteers started enrolling, with results expected mid-2020. [81]

CROI 2020 includes an oral presentation on combinectin. [109]

ABX464 - Rev inhibitor

ABX464 is an anti-inflammatory molecule thought to work by blocking the end stages of viral assembly.

HIV research is looking at strategies with compound to reduce the viral reservoir. The only other going studies related to use for ulcerative colitis, Crohn's disease and arthritis.

CROI 2020 includes a poster on ABX464 reducing HIV transcription and the viral reservoir. [110]

BIT225 - VPU

BIT225 is currently in phase 2 studies.

It is different to other experimental HIV drugs because it targets cells like macrophages and so is being used in addition to conventional ART to see whether it can reduce the viral reservoir.

CROI 2020 includes a poster on a phase 2 study of BIT225 in addition to ART. [111]

Development stopped or on hold

GS-9131 - NRTI

GS-9131 is an NRTI that is no longer being actively developed by Gilead.

CROI 2020 includes a poster on susceptibility of GS-9131 to drug resistant HIV-2. [112]

GS-PI1 - protease inhibitor

GS-PI1 is a once-daily unboosted protease inhibitor that is no longer being actively developed by Gilead.

Conclusion

Although there are now fewer large companies bringing new HIV drugs to market, Gilead, GSK/ViiV and Merck/MSD are all have long-acting molecules that cover both treatment and prevention, see Table 4. They are also all running studies of dual-therapy ART.

Although Janssen are not developing new HIV treatments their HIV vaccine is currently in two large phase 3 studies.

It is notable that these companies are also focused on targeting the HIV reservoir and related cure research.

If successful, the compounds in the pipeline report should dramatically reduce HIV incidence and provide better treatment for people living with HIV who for whatever reason have difficulty with daily oral medicines. (See Table 5).

Table 4: Compounds with long-acting formulations

Compound	Company
cabotegravir	ViiV Healthcare
islatravir	Merck/MSD
MK-8504 / MK-8583	Merck/MSD
bNAbs: including 3BNC117 and 10-1074; PGDM1400 and PGT121, 10E8.	Various including NIH/NIAID, Rockefeller University, ViiV Healthcare, Gilead Sciences.
GS-6207 (capsid)	Gilead Sciences
GSK '937 (maturation)	ViiV Heathcare
combinectin	ViiV Heathcare
elsulfavirine	Viriom

Table 5: Likely positioning for new drugs

Indication	Name
treatment-naive	islatravir, doravirine/islatravir
switch options on ART	islatravir, doravirine/islatravir, cabotegravir LA/ rilpivirine LA, bNAbs,
multidrug resistance (MDR)	islatravir, bNAbs, new classes: capsid and maturation inhibitors.
PrEP	cabotegravir-LA; islatravir; VRC01, all other mAbs.
maintenance without ART	bNAbs - in combinations as switch after viral load suppressed on ART.

References

References are generally to earlier reports in HIV Treatment Bulletin (HTB). Direct links to the original source documents are included in these reports. Full references are included in the main piplein report.

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