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PEACH

Pomalidomide as an immune-enhancing agent to control HIV

Pre-clinical data and clinical trial design: Maya D. Schou[1], Rachel D. Pascoe[1,2], Thomas A. Rasmussen[1,2,3]

Pre-clinical data

Pomalidomide

Pomalidomide is an immune-modulating imide drug (IMiD). The immune-enhancing effects are mediated by binding to cereblon which subsequently increase T cell expression of IL-2. Pre-clinical studies conducted on samples from people living with HIV demonstrates that pomalidomide enhances anti-HIV immunity ex vivo.

HIV-specific CD8+ T cells

Pomalidomide treatment drove an expansion of HIV-specific tetramer positive CD8+ T cells out of the total population of CD8+ T cells (Figure 1.A).

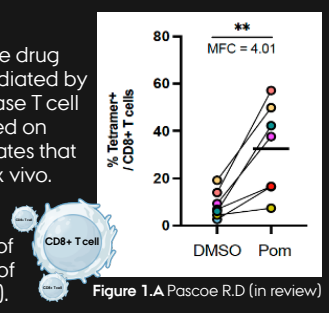


Figure 1.A Pascoe R.D (in review)

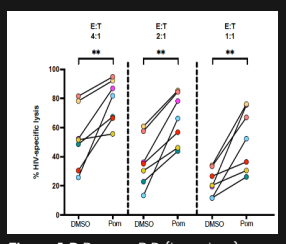


Figure 1.B Pascoe R.D (in review)

HIV-specific lysis

Pomalidomide treatment increased CD8+ T cell mediated lysis. Lysis was measured as a relative loss of peptide loaded CD4+ T cells (figure 1.B)

Pre-clinical data

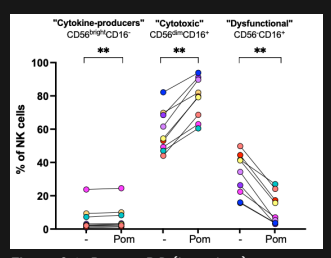
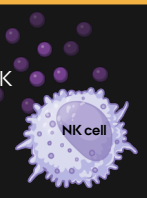


Figure 2.A Pascoe R.D (in review)

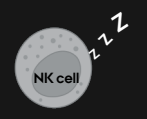
Cytotoxic NK cells

Pomalidomide expand cytotoxic NK cells as compared to DMSO (Figure 2.A) and increased NK cell polyfunctionality.



Dysfunctional NK cells

Pomalidomide reduced the frequency of dysfunctional CD56-CD16+ NK cells (Figure 2.A)



NK cells killing capacity

Pomalidomide Increased NK cell killing of K562 cells (Figure 2.B) and autologous in vitro infected CD4+ T cells (2.C)

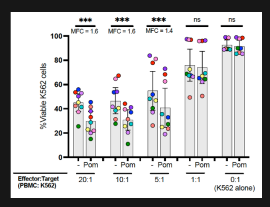


Figure 2.B Pascoe R.D (in review)

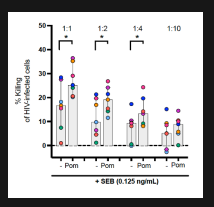


Figure 2.C. Pascoe R.D (in review)

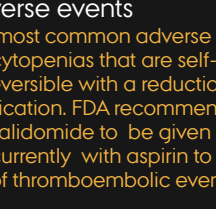
Trial sites

Aarhus University Hospital (DK): n =19
Monash Health (AUS): n = 3
Royal Melbourne Hospital (AUS): n =10

Safety

FDA approved

Pomalidomide is approved for the treatment of relapsed/ refractory multiple myeloma and Kaposis sarcoma.



Adverse events

The most common adverse events are cytopenias that are self-limiting or reversible with a reduction in medication. FDA recommends pomalidomide to be given concurrently with aspirin to mitigate the risk of thromboembolic events.

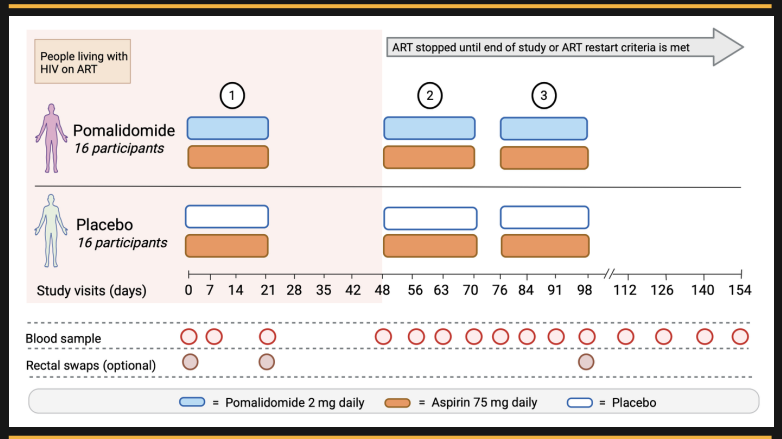
Outcomes

1. Safety
   Adverse events > grade 2 related to study therapy
2. Efficacy
   Time from ART cessation to meeting ART restart criteria
2. HIV reservoir
   Total and intact HIV DNA, CA-US and CA-MS HIV RNA
2. Immune cell profiles
   CD8+ T cell and NK cell characterisation and functionality.

Study design

Randomization

Participants will be randomized 1:1 to recieve either pomalidomide 2 mg/day or matching placebo, given concurrently with aspirin 75 mg, for three treatment cycles each consisting of 21 days.



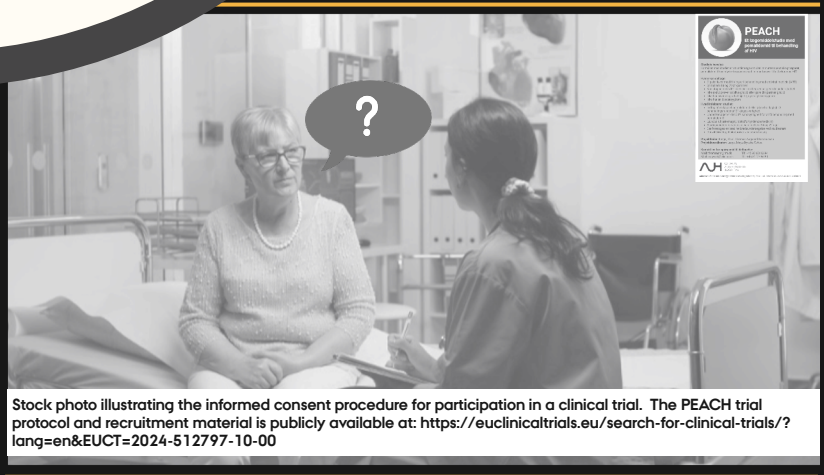
Study overview

A phase I/IIb clinical trial of pomalidomide in otherwise healthy PLWH on ART. Participants will receive treatment cycle I while on suppressive ART. Treatment cycle II and III will be given in the setting of an analytical teatment interruption (ATI). The ATI is scheduled to be 15 weeks or until ART restart criteria is met.

ART restart criteria

Confirmed HIV RNA >100,000 copies/mL, HIV RNA >1,000 copies/mL for 4 weeks, CD4+ T cell count <350 cells/uL or CD4+ T cell percentage <15%.

What's next?



Stock photo illustrating the informed consent procedure for participation in a clinical trial. The PEACH trial protocol and recruitment material is publicly available at: https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2024-512797-10-00

Site initiation

The trial site at Aarhus University Hospital (DK) was initiated in December 2024. Both Australian sites are expected to be initiated in autumn 2025.

Recruitment status

Recruitment started March 2025 at Aarhus University Hospital (DK). Currently there are 3 participants included in the PEACH trial.

Adverse event status

Adverse events have so far been mild and self-limiting.

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Acknowledgments: Thank you to our collaboration partners, founders and most importantly to all the people with HIV who contributed their time and effort by participating in research studies to advance our knowledge of HIV.

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