ID Week 2022 Report Back

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Outline

1. Hepatitis B Vaccination with HepB-CpG*:* BEe-HIVe preliminary results

2. Real World Outcomes in Injectable Cabotegravir-Rilpivirine

3. Single dose Liposomal Amphotericin B for Disseminated Histoplasmosis

Disclosures

No conflicts of interest or relationships to disclose.

Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

BEe-HIVe Preliminary Results

Background

- HBV vaccine seroprotection rates (SPR) in PWH are significantly lower (range 18-71%) than in adults without HIV (range 60-80%)[1]

- HepB-CpG vaccine *(Heplisav-B®)* is a 2-dose series (≥ 4w apart) for adults ≥ 18 FDA approved in 2017
  - In immunocompetent adults, SPRs with Hep B vaccine (*Engerix-B®* or *Recombivax-B®)* ranged from 65-80% vs. 90-95% with HepB-CpG[2]

- A single center study of 51 PWH, without immunity to hepatitis B, receiving HepB-CpG demonstrated overall SPRs of 82%, with higher SPR in those with higher CD4 cell counts[2]

1-National HIV Curriculum. 2-Schnittman S, JAIDS, 2021.

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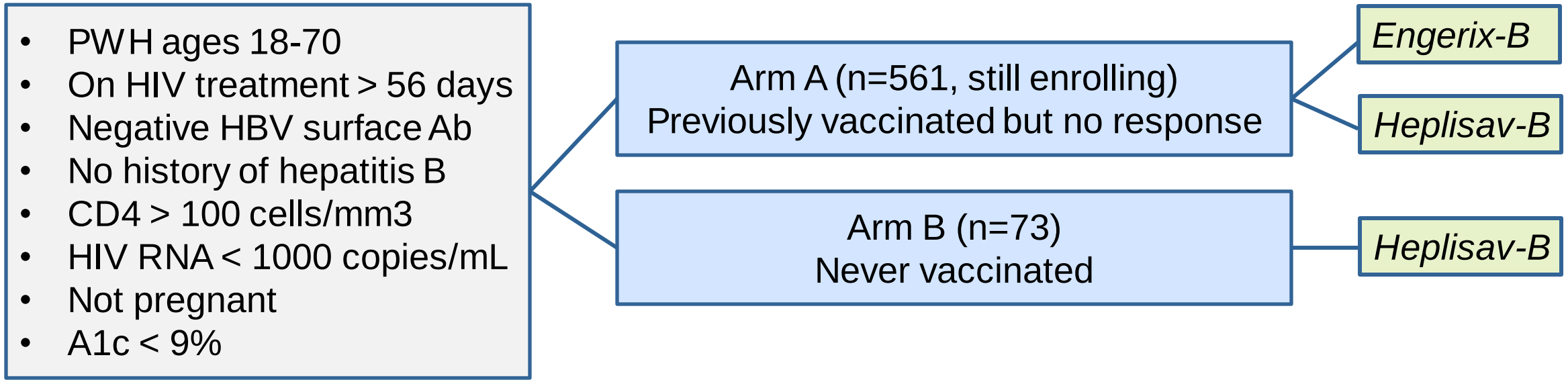
BEe-HIVe Study

- A5379 is an ongoing, prospective phase III open label RCT with the goal to evaluate the safety and immunogenicity of HepB-CpG in adults 18-70 years age

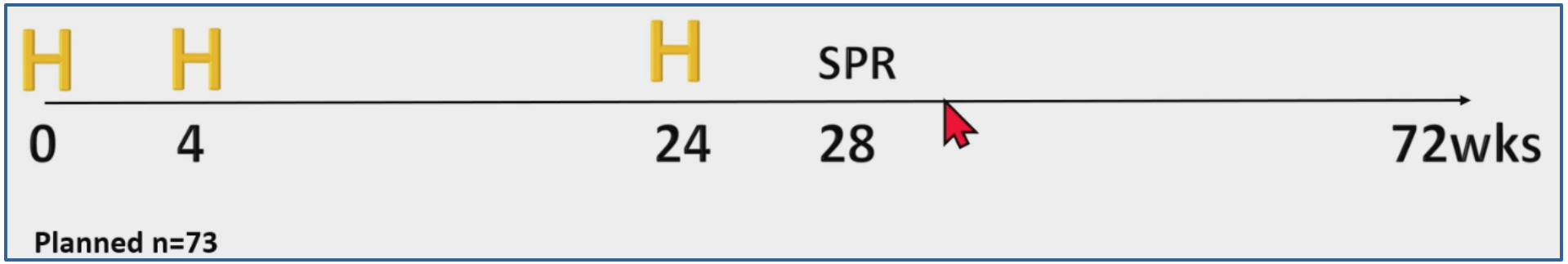


Marks K et al, ID Week 2022, #LB749.

BEe-HIVe Arm B Methods

- Objectives
  1. Determine 28w SPR (HBsAb ≥ 10 mIU/mL) of 3-dose regimen in HBV vaccine-naïve PWH
  2. Describe grade ≥ 3 adverse events

- HepB-CpG given at entry, 4 weeks, and 24 weeks; followed for 72 weeks



BEe-HIVe Arm B Patient Characteristics

Table 7.1: Baseline Demographics

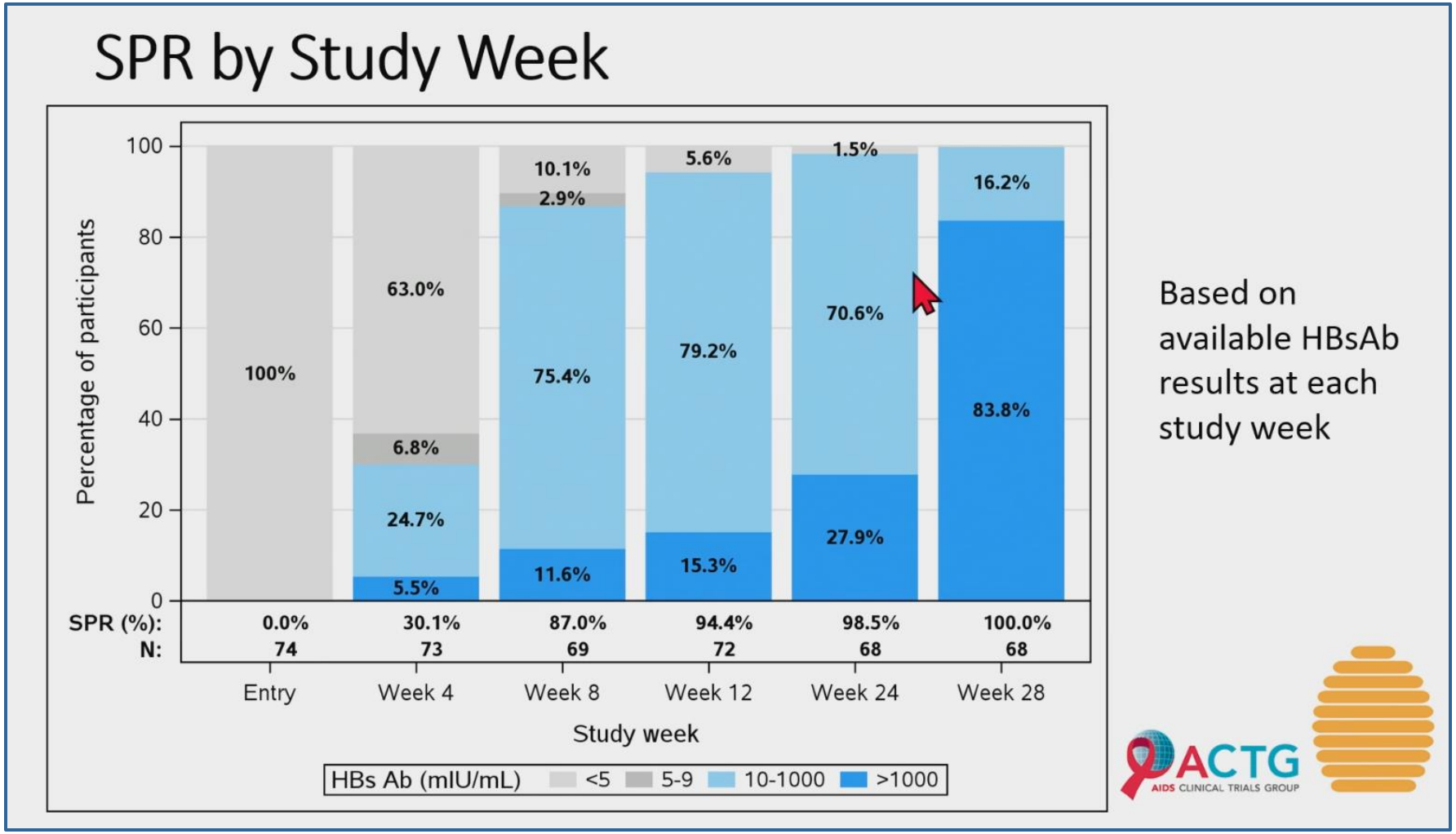
		GROUP B (N=74)
Age	Median (Q1, Q3)	47 (40, 51)
	Min, Max	23, 68
Sex at birth	Male	34 (46%)
	Female	40 (54%)
Gender Identity	Male	32 (43%)
	Female	40 (54%)
	Gender Queer	2 (3%)
Race	Asian	49 (66%)
	Black Or African American	12 (16%)
	White	11 (15%)
	Native Hawaiian Or Other Pacific Islander	1 (1%)
	Unknown	1 (1%)
Ethnicity	Hispanic Or Latino	11 (15%)
	Not Hispanic Or Latino	63 (85%)
Country	Thailand	48 (65%)
	United States Of America	20 (27%)
	South Africa	6 (8%)
IVD user	Never	74 (100%)
Smoking status	Current	9 (12%)
	Former	24 (32%)
	Never	41 (55%)

Table 7.3: Baseline HIV-Related Characteristics

		GROUP B (N=74)
Nadir CD4 (cells/mm³)	Median (Q1, Q3)	247 (140, 429)
	Min, Max	10, 933
	# Missing	0
Nadir CD4 (mm³)	<50	11 (15%)
	50 - <200	17 (23%)
	200 - <500	32 (43%)
	500+	14 (19%)
CD4 Count (cells/mm³)	Median (Q1, Q3)	625 (473, 829)
	Min, Max	1, 1562
	# Missing	0
HIV-1 RNA (copies/mL)	<60	71 (96%)
	60+	3 (4%)

Marks K et al, ID Week 2022, #LB749.

BEe-HIVe Arm B Results



Marks K et al, ID Week 2022, #LB749.

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BEe-HIVe Arm B Results

- Of 74 PWH in Arm B, 68 PWH completed 3 doses of HepB-CpG vaccine and had a HBsAb measurement
  - 100% SPR (95% CI: 94.7-100%)
  - 88.2% achieved HBsAb ≥ 1000 mIU/mL

- SPR was also evaluated after the 2nd dose of HepB-CpG vaccine
  - 94% achieved SPR 8 weeks after 2nd dose
  - 98.5% achieved SPR 24 weeks after 2nd dose

Marks K et al, ID Week 2022, #LB749.

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BEe-HIVe Arm B Adverse Effects

- 61% of participants experienced one or more AEs related to study participation
  - Grade 1 = 39% of participants
  - Grade 2 = 20% of participants
  - Grade 3 (malaise) = 1 participant

Adverse Effects	Percent of Participants
Injection site reaction	40%
Malaise	26%
Fatigue	23%
Myalgia	22%
Headache	22%
Fever	3%

Marks K et al, ID Week 2022, #LB749.

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BEe-HIVe Arm B Preliminary Results: Summary

- In this single arm study, 100% of 68 HBV vaccine naïve PWH after 3-dose HepB-CpG (*Heplisav-B*®) achieved SPR (HBsAb ≥ 10 mIU/mL)
- There were no unexpected safety issues or deaths
- Low representation from predictors of non-response (low CD4, viremia, HCV)
- **Unfortunately, 2 dose HepB-CpG was not the protocol used in this study**

Real World Outcomes with LAI CAB-RPV

Real World Outcomes: LAI Cabotegravir-Rilpivirine

- Sension et al - Real World Use and Effectiveness in the US in the 1st Year
- Welford et al - Low level HBViremia in PWH with Isolated HepBcAb After Switch
- De Wit S et al – CARISEL: Implementation Effectiveness in EU Clinical Sites

Real World Use & Effectiveness of LA CAB-RPV in OPERA Cohort

- Among OPERA cohort (~145,000 PWH in 96 clinics in the US), 383 ART experienced PWH received 1st dose IM CAB-RPV between 1/2021-2/2022
  - 84% HIV-1 RNA < 50 copies/mL, 7% HIV-1 RNA 50-200 copies/mL, 7% HIV-1 RNA > 200 copies/mL, 2% no baseline HIV-1 RNA

- 89% remained on therapy in the study period
  - 95% of those who were UD at baseline remained UD
  - 91% who were viremic at initiation (21) achieved viral suppression

- Assessing oral intake was difficult to determine because of different ways to bridge and lead-in & poor documentation in the EHR

Sension MG et al, ID Week 2022, #1582.

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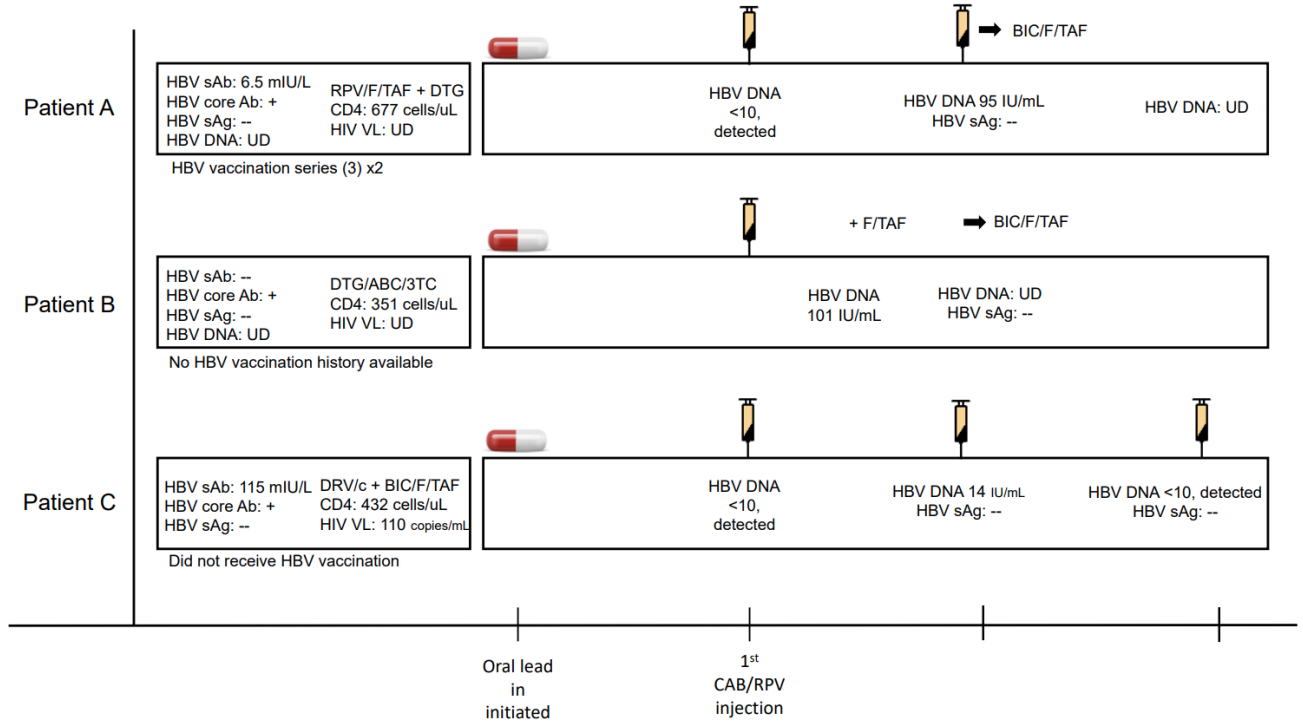
Low Level HBViremia after Switch to CAB-RPV in Isolated HBcAb

- Retrospective case series of 149 PWH switched to LAI CAB-RPV
  - 25.5% (38/149) isolated hep B core antibody positive
  - 7.9% (3/149) with HBV viremia, clinical significance of which is unknown

Figure 1. Baseline patient characteristics and timeline trend of hepatitis B DNA and hepatitis B surface antigen levels following a switch to long-acting injectable cabotegravir/rilpivirine.



Welford et al, ID week 2022, #1583.

CARISEL: Implementation of LAI CAB-RPV in the EU

- ViiV sponsored phase 3b multicenter open-label implementation-effectiveness trial examining strategies to support implementation across 5 EU countries
  - 437 participants at 18 clinical sites with 70 staff providers

- Comparing standard arm to enhanced implementation
  - Standard arm = Education resources, virtual injection training, regular support
  - Enhanced arm = Face-to-face injection training, CQI, educational resources

- Month 12 endpoints
  - Viral suppression 87% across both arms
  - Suggests that "regardless of implementation support and clinical infrastructure CAB + RPV LA can be highly effective for a wide variety" of PWH

De Wit S et al, ID Week 2022, #1584.

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High Dose L-AmB for Disseminated Histoplasmosis

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Background: Histoplasmosis in PWH

- Histoplasmosis is endemic to central & south-central US and Latin America
- PWH with CD4 < 150 cells/mm^3 have an increased risk of dissemination

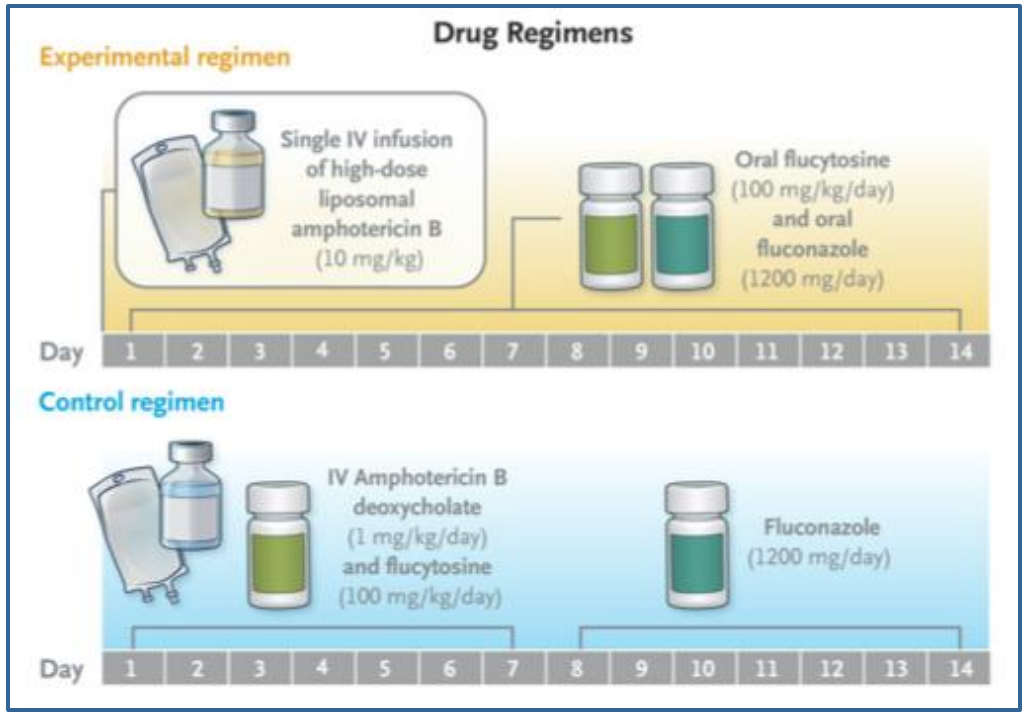
Table 11. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV

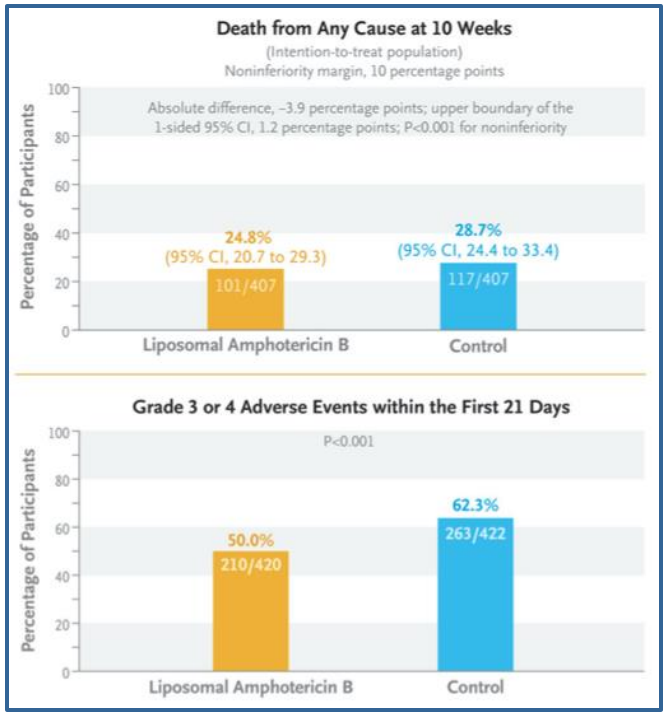
Treatment of Disseminated Histoplasmosis
Treating Moderately Severe to Severe Disseminated Disease
Induction Therapy **Preferred Therapy:** • Liposomal amphotericin B at 3 mg/kg IV daily (**AI**) **Alternative Therapy:** • Amphotericin B lipid complex 5 mg/kg IV daily (**AIII**) **Duration:** • For at least 2 weeks or until clinically improved
Maintenance Therapy **Preferred Therapy:** • Itraconazole 200 mg PO three times daily for 3 days, then twice daily for at least 12 months (**AII**), with dosage adjustment based on interactions with antiretroviral medications and results from itraconazole serum concentration

National HIV Curriculum.

Background: Histoplasmosis in PWH

- Treatment of histoplasmosis is onerous and often not readily accessible
- Recently, the AMBITION trial demonstrated that a one-time high-dose of liposomal amphotericin B (L-AmB) was non-inferior to 2 weeks induction with amphotericin B for treatment of cryptococcal meningitis in PWH





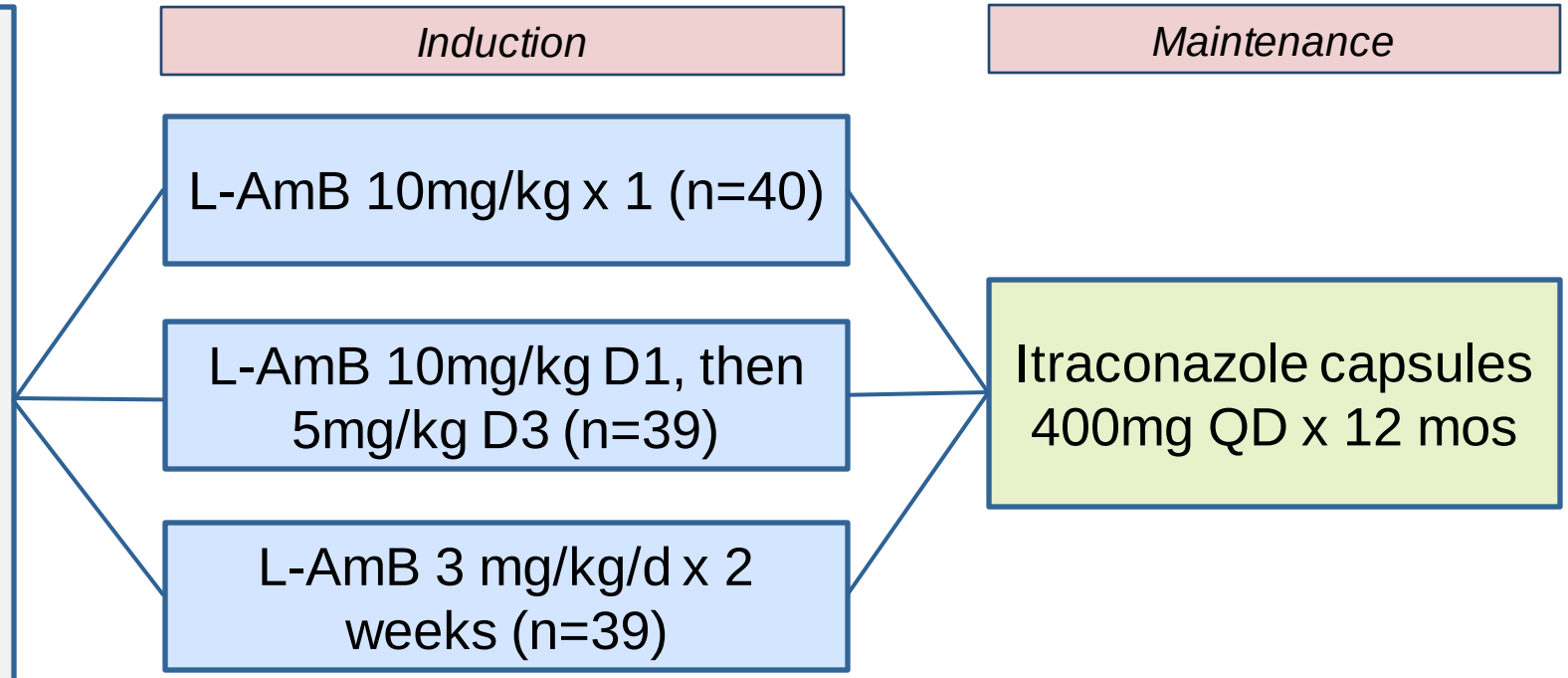
Jarvis JN et al, NEJM, 2022.

Methods: Single Dose L-AmB for Disseminated Histoplasmosis

- Prospective randomized phase II open label multicenter study in Brazil of induction therapy options for disseminated histoplasmosis

PWH with disseminated histoplasmosis expected to live for >48 hours WITHOUT:

- Prior hx of histoplasmosis
- Pregnancy
- Tuberculosis
- CNS histoplasmosis
- Renal insufficiency
- Receipt of a polyene antifungal in the 48h prior



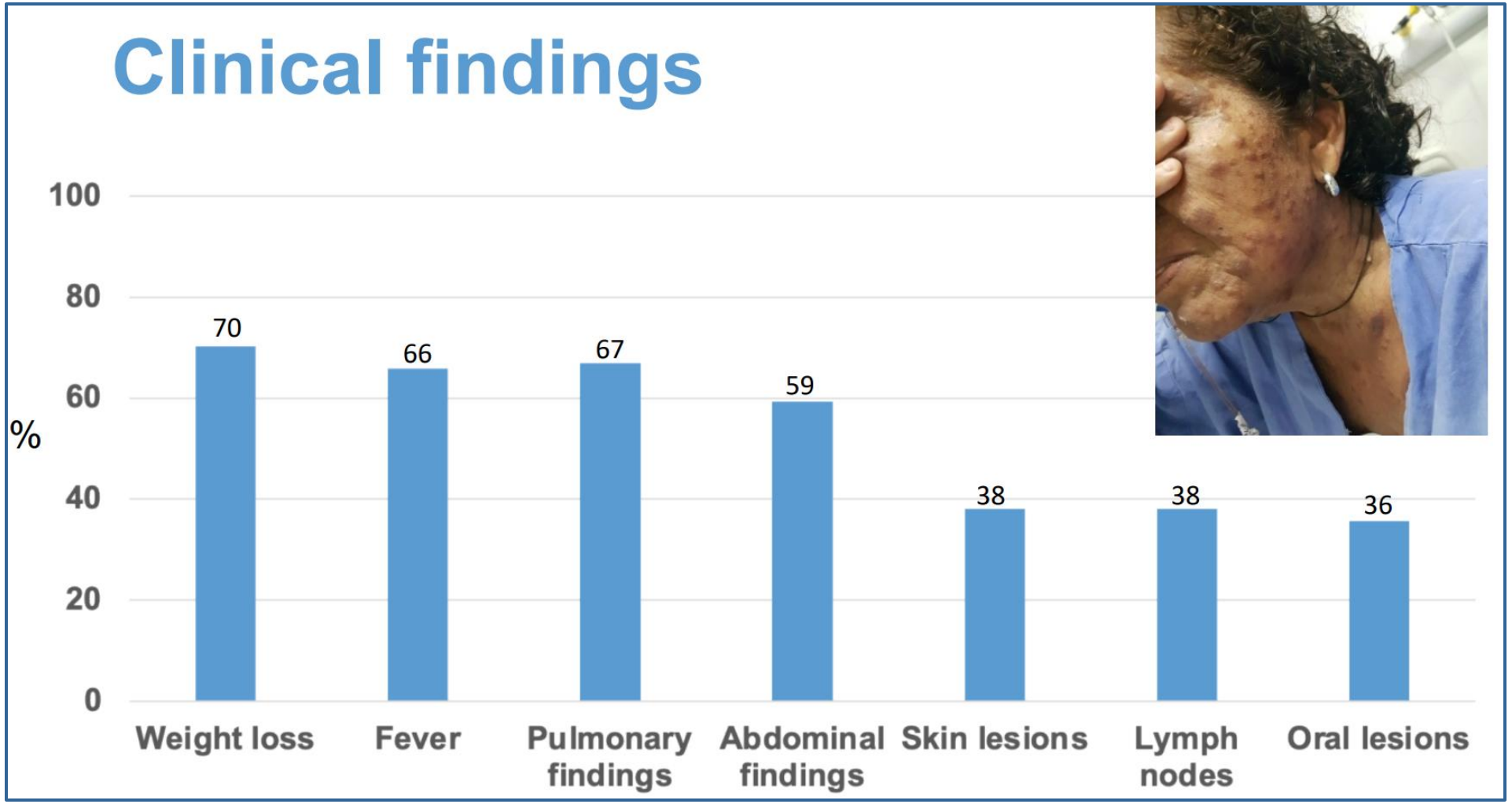
Pasqualotto AC et al, ID Week 2022, #LB 2303.

Methods: Single Dose L-AmB for Disseminated Histoplasmosis

- Primary Endpoint
  - Clinical response @ day 14
    - Resolution of fever AND signs/symptoms attributable to histoplasmosis

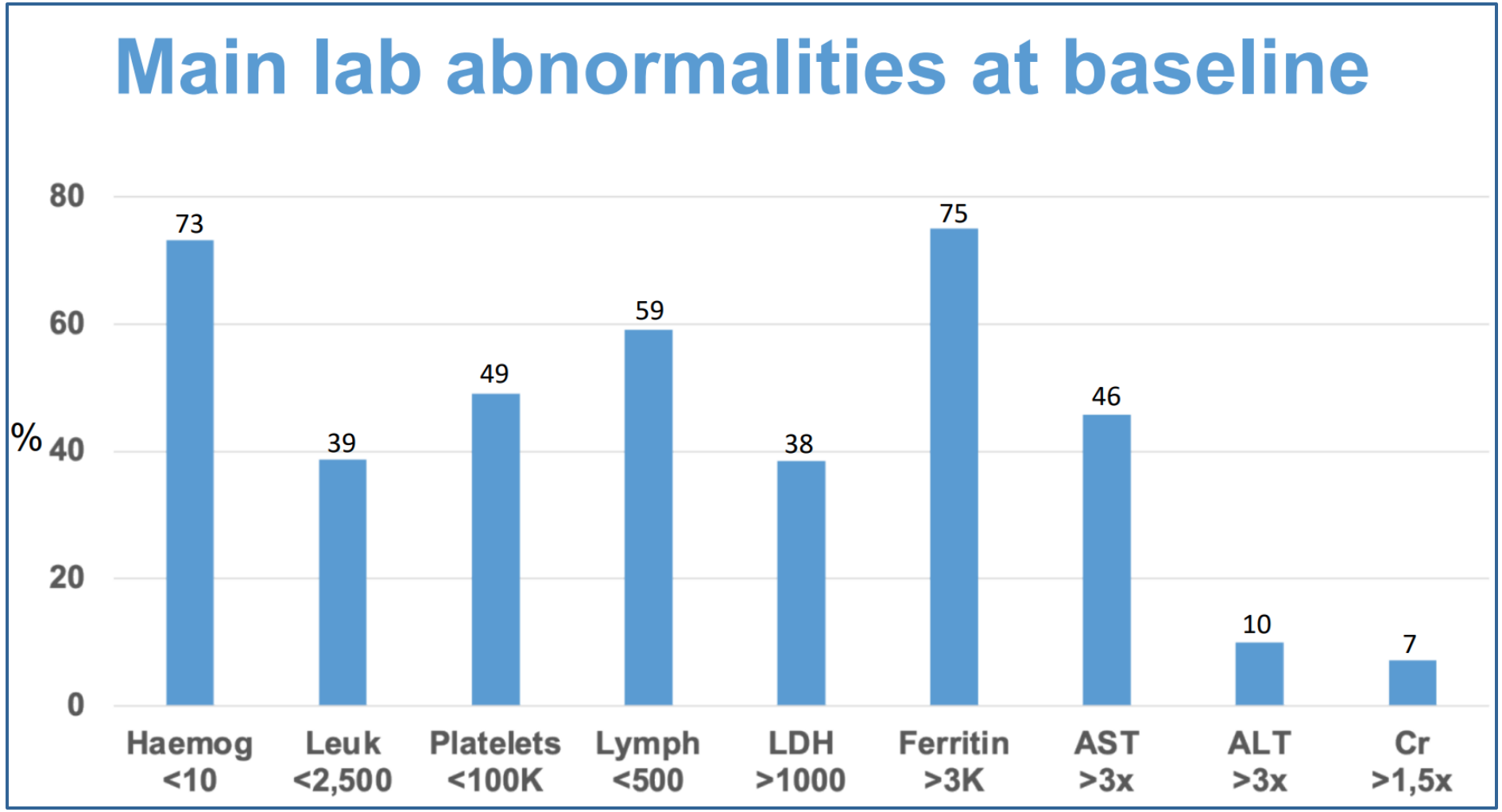
- Secondary Endpoints
  - Overall mortality @ day 14
  - Renal function abnormalities

Results: Clinical Findings at Study Entry



Pasqualotto AC et al, ID Week 2022, #LB 2303.

Results: Laboratory Abnormalities at Study Entry



Pasqualotto AC et al, ID Week 2022, #LB 2303.

Results: Diagnostics Methods Used for Study Entry

Pasqualotto AC et al, ID Week 2022, #LB 2303.

Results

- Characteristics, symptoms, laboratory abnormalities similar between arms
  - Age ~40 years
  - Mostly male (70-88%)
  - Median CD4 25 cells/mm^3
- Clinical response @ day 14
  - Arm 1 82%, arm 2 68%, arm 3 72%, but no difference in ARR
- Similar toxicities, if not better in Arm 1, with regard to infusion-related symptoms, kidney abnormalities, anemia, etc.

Pasqualotto AC et al, ID Week 2022, #LB 2303.

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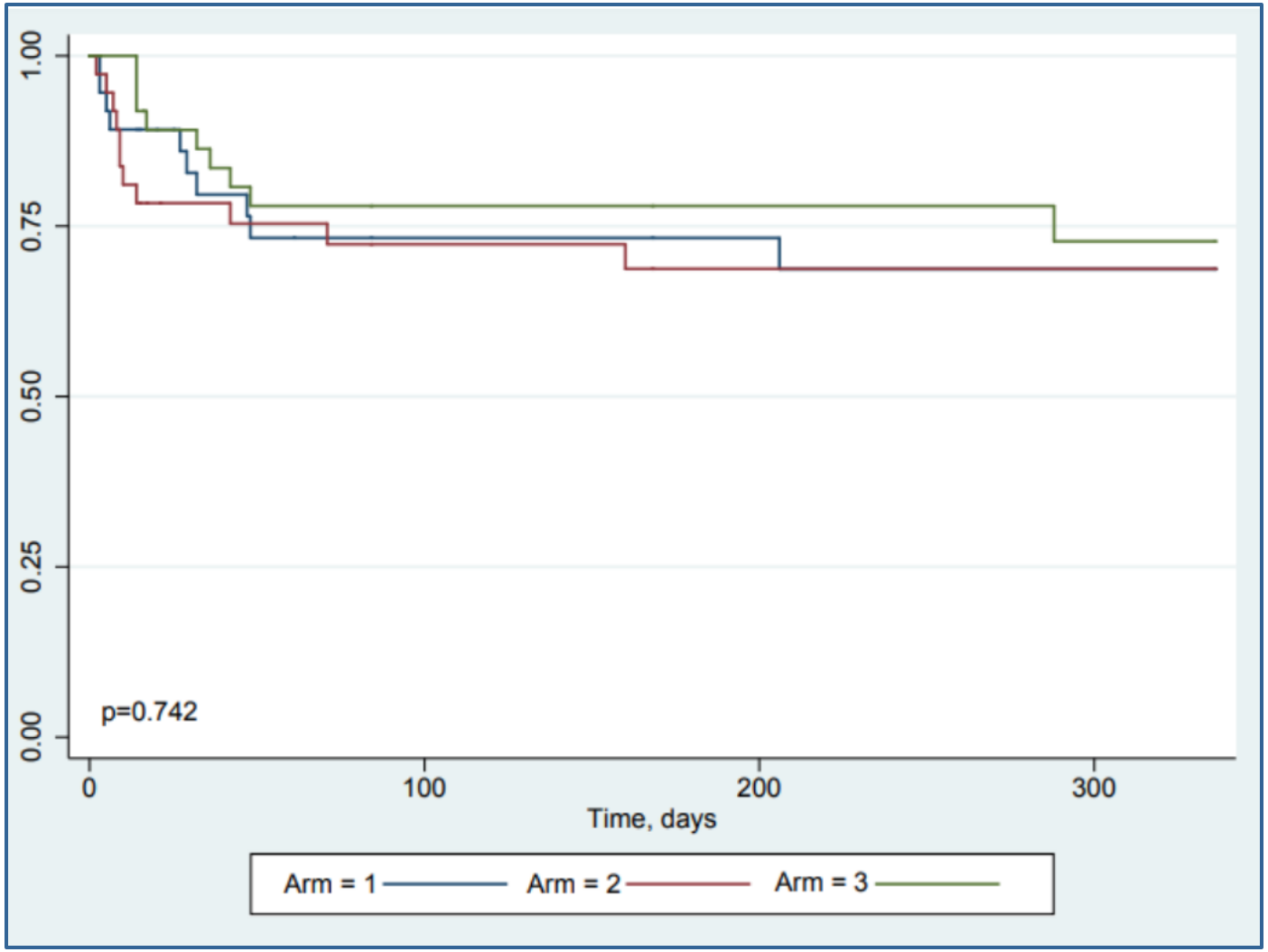
Results: Cumulative Probability of Survival



Pasqualotto AC et al, ID Week 2022, #LB 2303.

Summary

- In a prospective randomized phase II open label study of L-AmB induction options for disseminated histoplasmosis, single high-dose L-AmB was non-inferior to standard of care for clinical response at day 14
- Toxicities were similar across the L-AmB arms
- **A Phase III trial is being planned, which has the potential to revolutionize treatment, and access to it, for PWH with disseminated histoplasmosis**

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