PEGINTERFERON ALFA-2A AND BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE IN NORTH AMERICAN ADULT T-CELL LEUKEMIA/LYMPHOMA (NA-ATLL): A PRELIMINARY REPORT

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Introduction

- **Adult T-cell leukemia/lymphoma (ATLL)** is a rare and aggressive CD4+ T-cell neoplasm caused by human T-lymphotropic virus type 1 (HTLV-I).
- In North America, ATLL poses particular challenges due to its **aggressive** nature and **limited treatment** options.
- Historically, **AZT combined with interferon-alpha** was the standard of care.
- Interferon-alpha has now been replaced, with **PEG-Interferon alpha 2a** and novel antiretrovirals available.
- Emerging data suggest that antiretroviral agents used in HIV treatment, such as **bictegravir-based regimens**, may suppress HTLV-I replication.
- These regimens may offer **therapeutic benefit** in ATLL management.

Objective

To evaluate the safety, tolerability, and preliminary efficacy of **peginterferon alpha-2a (PEG-IFN)** in combination with **Biktarvy (bictegravir/ emtricitabine/tenofovir alafenamide)** in a North American ATLL cohort.

Methods

- **Patients:** 5 adults with ATLL (1 chronic, 2 lymphomatous, 2 acute).
- **Treatment:** PEG-IFN alpha-2a (180 mcg SC weekly, avg. 11.8 cycles; range 3–24) + daily Biktarvy.PEG-IFN alpha
- **Additional therapy:** Venetoclax (n=1), Mogamulizumab (n=1).
- **Outcomes assessed:** Overall response rate (ORR), adverse events (AEs), HTLV-I proviral load, ATLL cell count.

Results

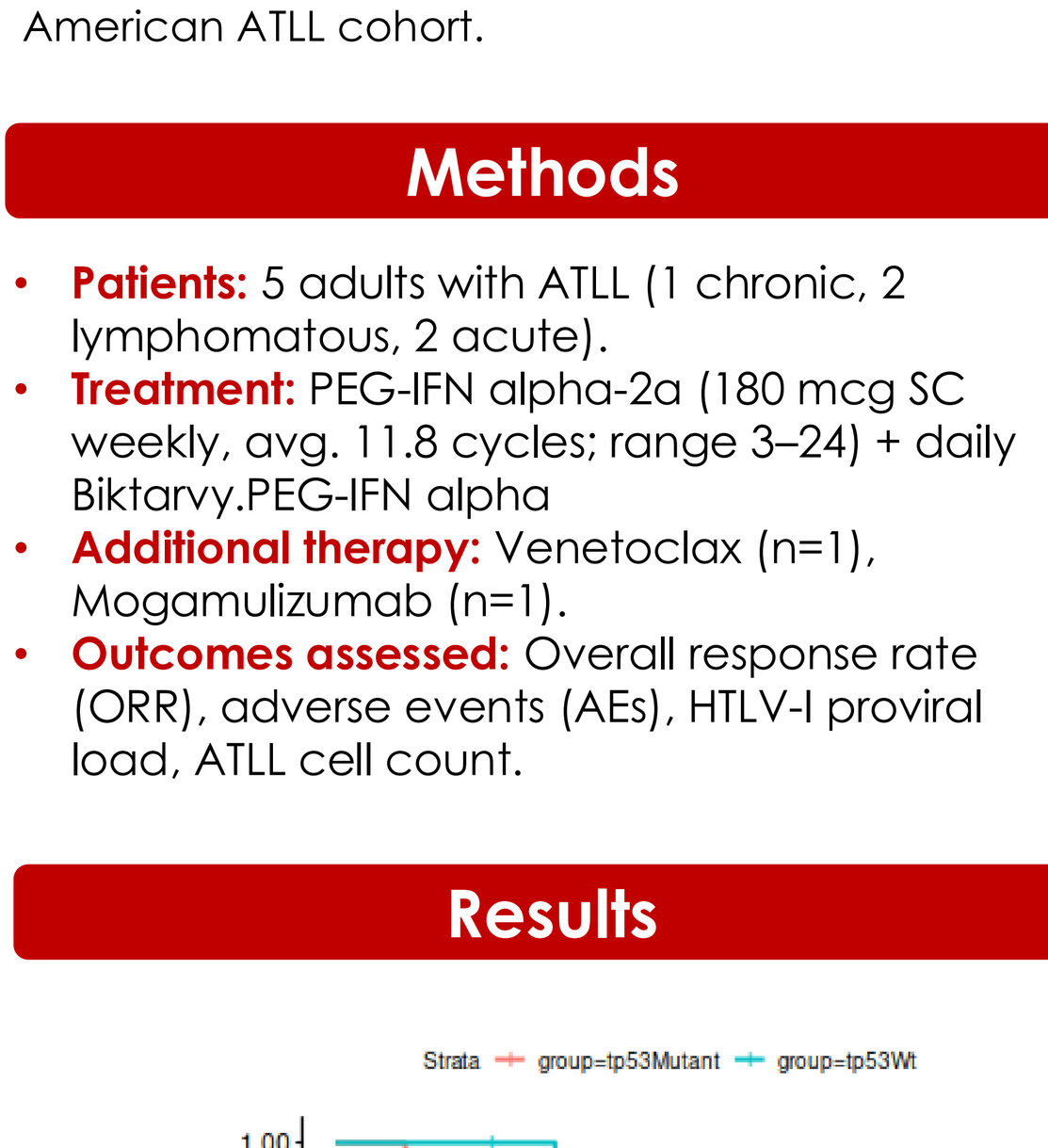


Figure 1: Venetoclax shows activity in R/R ATLL. Mutational analysis reveals 44% (4 out of 9) of our patients had TP53 mutations. These patients had a worse prognosis than TP53 wild-type cases (mean OS in TP53 mutants: 40 days versus 255 in wild-type patients. There was a significant difference between the two cohorts with a log rank p-value of 0.0027.

Results, cont'd

Case #	Shimoyama Type	Mutational Profile	Lines of Therapy	Best response	Overall Survival (days)	Cause of Death
1	Lymphomatous	FAS, GATA3, NOTCH1, P2RY8, REL, B2M	1. EPOCH x6 (Relapsed) 2. ICE x1 (Relapsed) 3. IFN/AZT (Relapsed) 4. Mogamulizumab (SD/Relapsed) 5. RT (PR/SD) 6. Decitabine/ venetoclax	Partial Response	137	Disease progression
2	Acute	CARD11, IDH2, POT1, TET2 AND TP53, BRCA2, EGFR, MALT1, TBL1XR1	1. CHOP (Relapsed) 2. ICE x2 (Relapsed) 3. ASCT/BEAM (SD/Relapsed) 4. Azacitidine/ venetoclax	Partial Response	26	CMV Pneumonia Disease progression
3	Acute	NTRK1, PBMR1, TP53	1. EPOCH x5 (Relapsed) 2. Decitabine/ venetoclax	Partial Response	28	Disease progression
4	Acute	ARID2, KLF2, TP53, ERBB2, KRAS, MYC, CD274/PD L1 (amplification)	1. EPOCH x1 (Relapsed) 2. ICE/venetoclax 3. Decitabine	Partial Response	54	Disease progression
5	Lymphomatous	ZFH4, EP300	1. EPOCHx4 Kinetic Relapse. No CR 2. CRISPR CTX130(X2)+RT. CR but relapsed 3 mo. 3. Decitabine +DHAP. 4. ICE+Venetoclax	Partial Response *resensitized	642	Disease progression
6	Acute	CARD11, CIC, BRCA2	1. EPOCHX2 (PD) 2. Deci/ICE NR 3. Cy/PEGIFNAZT/ VEN	Progressive Disease	82	Sepsis
7	Lymphomatous	NA	1. EPOCHX2. 2. Deci ICE 3. CRISPRCTX130. 4. Deci-ESHAP	Partial Response *resensitized	162	Sepsis Intestinal rupture Disease progression
8	Acute	FAT1, TBL1XR1,BR CA2, TP53	1. ICE 2. EPOCH 3. ALRN Clinical Trial 4. DeciVEN	Progressive Disease	52	Liver failure Disease progression
9	Acute	PLCG1, ATG2B,EGF R,KMT2C, PMS2	1. EPOCHX1 2. Decitabine + ESHAP 3. PEG-IFN+ Biktarvy and VEN	Complete Response	Alive (+90 days)	NA

Table 1: The addition of HMA/venetoclax to chemotherapy was well-tolerated. The main adverse effects were: cytopenias, fatigue, infections/sepsis. Overall response rate was 77%; we observed one CR, 6 PRs, and 2 patients exhibited POD.

Discussion

- This first North American experience with **PEG-IFN + Biktarvy** in ATLL shows **promising clinical activity**
- Treatment was **tolerable with manageable toxicity**
- Patients achieved **meaningful virologic and hematologic responses**
- Findings suggest this regimen may have utility in both **induction and maintenance therapy**
- Results provide rationale for **future prospective clinical trials** in ATLL

References

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