PEVONEDISTAT (TAK-924): A POTENTIAL NEW TREATMENT FOR HR-MDS AND AML

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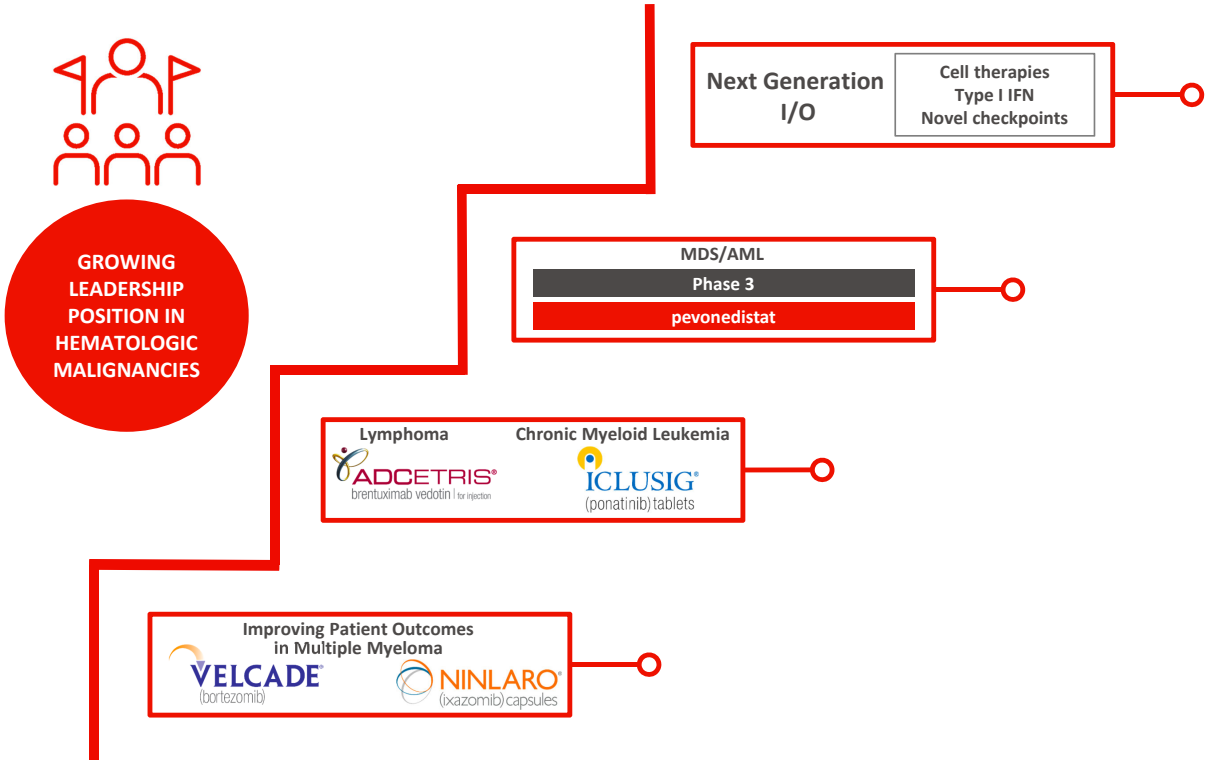
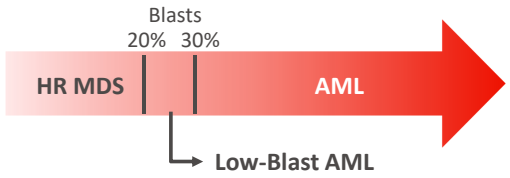
Better Health, Brighter Future

BUILDING ON THE TAKEDA ONCOLOGY FOUNDATION IN HEMATOLOGIC MALIGNANCIES



HIGH RISK MYELODYSPLASTIC SYNDROME (HR-MDS) AND ACUTE MYELOID LEUKEMIA (AML) HAVE LIMITED TREATMENT OPTIONS

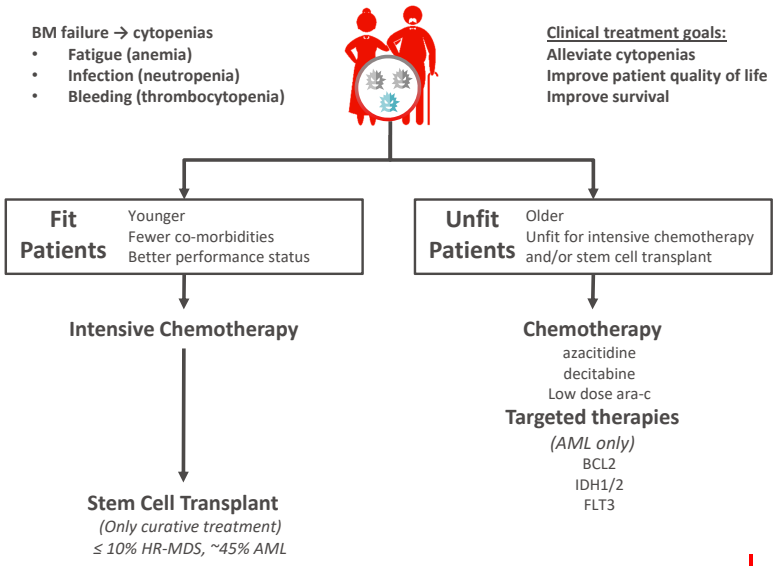
CONTINUUM OF HR-MDS AND AML



- HR-MDS and AML are both rare bone marrow-related cancers that share foundational biology, clinical features, and genetic mutations*
- Incidence highest in elderly (>70 years old)
- Overall survival several months to a few years, depending on risk category

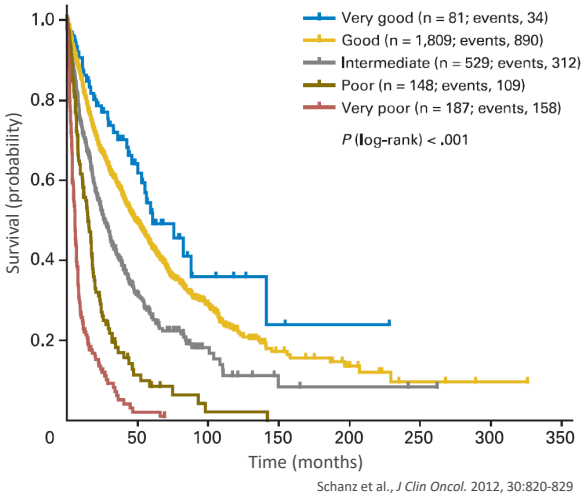
* 30% of HR-MDS patients progress to AML

CLINICAL TREATMENT



CURRENT STANDARD OF CARE IS INADEQUATE FOR HR-MDS PATIENTS

MDS SURVIVAL BY PROGNOSTIC RISK



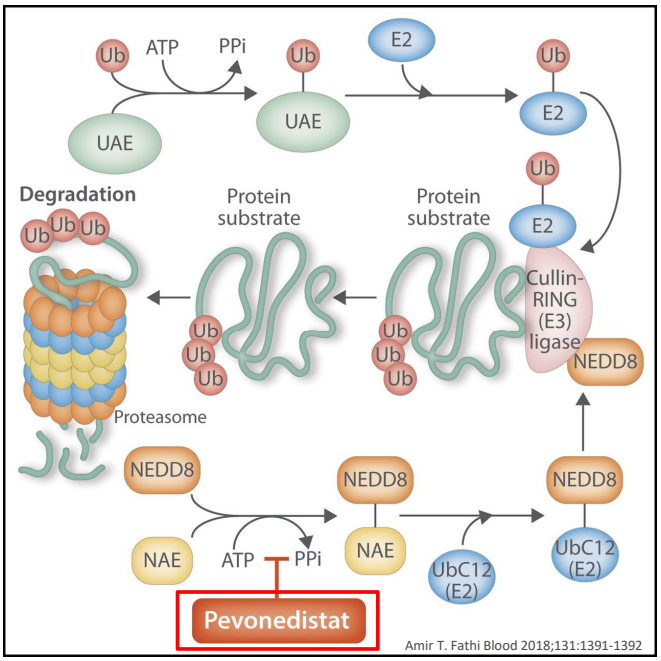
Schanz et al., *J Clin Oncol.* 2012, 30:820-829

Median survival ~6 months to 5 years

- No new treatments have been approved for MDS in over a decade
- Transplant ineligible patients treated with first line therapy: Median OS = 15mo; 2yr OS rate 35%
- Economic burden is substantial - hospitalizations are common among patients and many are transfusion dependent

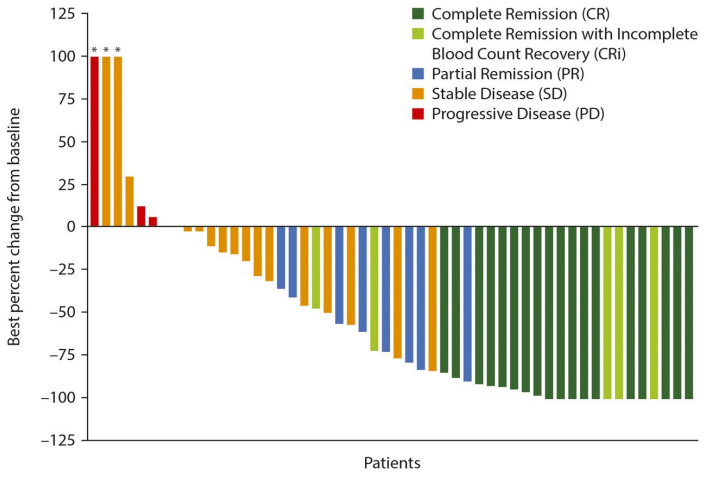
PEVONEDISTAT: A UNIQUE FIRST-IN-CLASS NAE INHIBITOR

- Pevonedistat is a small molecule inhibitor of NAE (NEDD-8 activating enzyme), a protein involved in the ubiquitin-proteasome system
- NAE acts upstream of the proteasome and catalyzes the first step in the neddylation pathway



ENCOURAGING RESPONSES IN AML PATIENTS TREATED WITH PEOVNEDISTAT + AZACITIDINE

Figure 1: Waterfall plot of best percent change from baseline in marrow blasts for the response-evaluable pts who received pev 20 mg/m² (n=52). Responses are listed as best responses achieved on study



*Best percent change from baseline >100%.
SD represents those evaluations which did not qualify for response or PD.

Ronan T Swords et al. Blood 2016;128:98

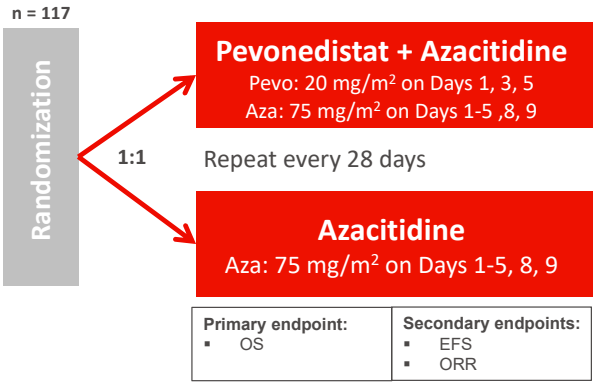
60% ORR with a trend towards improved survival in secondary AML

Response rates not influenced by AML genetic risk or leukemia burden

Initial data drove interest to move to registration

A PHASE 2 STUDY IN HR-MDS TO CONFIRM THE RISK / BENEFIT PROFILE OBSERVED IN AML

Phase 2, Randomized, Open-label, Global, Multicenter Study Comparing Pevonedistat Plus Azacitidine vs. Azacitidine in Patients with Higher-Risk MDS, CMML, or Low-Blast AML

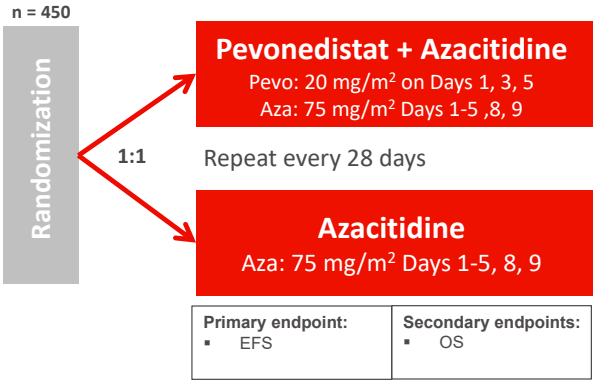


- Mature OS data will be available in November
- Data will be presented in upcoming congress
- Potential approval in FY21*

* Projected approval date assumes filing on Phase 2 data

THE PHASE 3 PANTHER STUDY WAS INITIATED AT RISK TO ACCELERATE DEVELOPMENT

Phase 3, Randomized controlled trial of Pevonedistat Plus Azacitidine Versus Single-Agent Azacitidine as First-Line Treatment for Patients with Higher risk-MDS/CMML, or Low-blast AML



PANTHER

- Completed global enrollment 10 months earlier than originally projected*
- Indicative of demand for new innovative therapies

* Closed to global enrollment; Open for extended enrollment in China

EXPANDING PATIENT-CENTRIC DEVELOPMENT OF PEVONEDISTAT

Continuum of disease

HR-MDS

Ph2 (P2001)

*Potential approval in FY21**

Ph3 (P3001)

PANTHER

NEW STUDIES IN UNFIT AML

Ph3 PEVOLAM

pevo + aza vs. aza
Currently enrolling patients

Utilizing partnership (PETHEMA) for efficient development

Ph2 (P2002) Combo

pevo + venetoclax + aza vs. venetoclax + aza
Study will open in 2020

Unique MOA and biologic hypothesis to support combination

* Projected approval date assumes filing on Phase 2 data

SUMMARY

1

Unmet need in High-risk MDS and AML remain high with few treatment options

2

Pevonedistat is a selective first-in-class inhibitor with potential to be first new therapy in over a decade for HR-MDS

3

The Ph2 HR-MDS trial has reached the updated OS endpoint data readout and the PANTHER Ph3 trial has completed global enrollment