KINTARA Therapeutics

Kintara's VAL-083: A First-in-Class Bifunctional Alkylating Agent with Promising Activity in MGMT Promoter-Unmethylated & Methylated Glioblastoma

10-December-2020

VAL-083 Mechanism of Action

- Unique MOA damages DNA across both of the strands inducing DNA inter-strand crosslinks leading to lethal double strand breaks
- VAL-083's unique cytotoxic mechanism circumvents MGMT-mediated chemoresistance and differentiates it from current therapies used in the treatment of GBM, including TMZ as SOC
- Effectively crosses the blood brain barrier
- Patients treated on days 1, 2, 3, of a 21-day cycle

**Dose to be studied in GAR GBM AGILE pivotaltrial*

Current Clinical Trials Overview

- Two Open-label Phase 2 clinical trials comprising three patient cohorts in MGMT-unmethylated GBM patients against historical controls
- Sun Yat-sen University Cancer Center (SYSUCC) Clinical Trial – fully enrolled
  - Newly-diagnosed [first-line] patients
    29 evaluable patients with **25 evaluable patients treated at 30 mg/m^2/day starting dose***
- MD Anderson Cancer Center (MDACC) Clinical Trial - ongoing
  - Recurrent patients
    77 evaluable patients with **43 evaluable patients treated at 30 mg/m^2/day starting dose***
  - Newly-diagnosed [adjuvant] patients
    27 evaluable patients, **all treated at 30 mg/m^2/day starting dose***

**Dose to be studied in GCAR GBM AGILE pivotal trial*

KINTARA Therapeutics

Efficacy Signal in All Three Cohorts

Newly Diagnosed Patients (MGMT-unmethylated)	Evaluable 30 mg Patients*	Median Progression Free Survival	Median Overall Survival
SYSUCC Newly Diagnosed [First Line]	n=25	8.7 months	18.2 months
MDACC Newly Diagnosed [Adjuvant]	n=27	10.0 months	16.5 months
TMZ Historical Comparator		*5.3-6.9 months*[1,2]	*12.7-16.0 months*[1,2]

Recurrent Patients (MGMT-unmethylated)	Evaluable 30 mg Patients*		Median Overall Survival
MDACC Recurrent	n=43		8.5 months
Lomustine Historical Comparator			*7.2 months*[3]

[1]*Hegi et al N Eng J Med 352; 997-1003 (2005)*
[2]*Tanguturi et al. NeuroOncol; 19(7): 908-917 (2017)*
[3]*Wick et al N.Eng.J.Med; 377:1954-1963 (2017)*

**Dose to be studied in GCAR GBM AGILE pivotal trial*
Data from SNO 2020 posters

GBM AGILE

Adaptive Global Innovative Learning Environment

Development of GBM AGILE

THE PROBLEM

The current trials in GBM pose the following shortcomings:

- Imaging-based endpoints can be misleading
- Historical control comparison can under- and overestimate treatment effect leading to bad decisions
- Different targets, different biomarkers for similar pathways
- Biomarker subgroups are not well defined
  - Overlapping genomic groups
  - No gold standard for MGMT

THE SOLUTION

Don't need to "re-create the wheel" for each trial

- Assemble GBM experts from around the globe to develop ideal phase II-III development plan
- Work with regulators to iron out details
- Create an ongoing infrastructure to limit downtime and enable institutional learning and knowledge
- Provide "turn-key" GBM development solution to biopharma

= GBM AGILE

GBM AGILE

GBM AGILE: A global, phase 2/3 adaptive platform trial to evaluate multiple regimens in newly diagnosed and recurrent glioblastoma

- GBM AGILE, Glioblastoma Adaptive, Global, Innovative Learning Environment, is a biomarker based, multi-arm, seamless Phase II/III Response Adaptive Randomization platform trial designed to evaluate multiple therapies in newly diagnosed (ND) and recurrent GBM with the goal of identifying effective therapies for glioblastoma and matching them accurately to differnet patient subtypes in an accelerated manner.
- It is a collaboration between academic investigators, patient organizations and industry to support new drug applications for newly diagnosed and recurrent GBM.
- Adaptive platform trials offer a unique ground for discovery and rapid testing of various experimental drugs, and create a more efficient and cost effective mechanism for accelerating treatment in GBM patients.
- GBM AGILE is sponsored by Global Coalition for Adaptive Research, a non-profit organization, whose mission is to speed the discovery and development of treatments for patients with deadly diseases and facilitate collaborations between patient groups, academic investigators and industry.

GBM AGILE

GBM AGILE: A global, phase 2/3 adaptive platform trial to evaluate multiple regimens in newly diagnosed and recurrent glioblastoma

ADAPTIVE: Design and trial structure that is adaptable based on response in participating patients.

GLOBAL: Global effort opens to a broad patient population with GBM across the world.

INNOVATIVE: Unique platform to make drug development cost effective and fasten the progress.

LEARNING **E**NVIRONMENT: Perpetual learning system to quickly add potentially promising new drugs and drop those that appear to be ineffective.

GBM AGILE

▶**Primary Objectives**

1. To identify experimental therapies that improve OS for GBM patients in the screening stage (Stage 1), determining if predefined patient subtypes or associated biomarkers uniquely benefit from the treatment.
2. To confirm identified efficacious experimental therapies and associated biomarker signatures in an expansion stage (Stage 2) designed to support a new drug application.

▶ **Secondary Objectives**

▶ 1. To evaluate Progression Free Survival by each biomarker/therapeutic combination.

▶ 2. To evaluate Overall Survival by each biomarker/therapeutic combination.

▶ 3. To determine short- and long-term safety signals and QOL measures

GBM AGILE – Trial Schema