Results of the NLG2105 phase 1 trial using the IDO pathway inhibitor indoximod, in combination with radiation and chemotherapy, for children with newly diagnosed DIPG

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Background

• The indoleamine 2,3-dioxygenase (IDO) pathway is a natural mechanism of immune suppression that tumors exploit to evade immune responses

• Indoximod is an orally administered, small-molecule IDO pathway inhibitor that reverses the immunosuppressive effects of the IDO pathway

• We hypothesize that immune activation using indoximod immunotherapy can allow responsiveness to chemotherapy and radiation in patients who would otherwise be refractory

• Indoximod impacts CD8+ T cells, CD4+ T helper cells, Tregs, and dendritic cells
  - Reverses the effects of low tryptophan by increasing proliferation of effecter T cells
  - Drives differentiation into Th1 helper cells vs Tregs
  - Downregulates IDO expression in dendritic cells

Phase 1 Study Schema

• Indoximod, in combination with up-front radiation therapy, followed by maintenance indoximod plus chemotherapy for pediatric patients with newly-diagnosed treatment-naive DIPG

Safety Data for DIPG Patients Treated on NLG2105

Success Rate and Representative MRI Results for DIPG Patients with Good Responses

Conclusions

• We show data supporting the hypothesis that some DIPG patients may benefit from indoximod-based multi-modal immune-radio-chemotherapy

• Adding indoximod to radiation for DIPG patients has been well-tolerated to date

• Most patients have had initial improvements in symptoms

• Inflammatory MRI changes may complicate treatment of newly-diagnosed DIPG

Future Directions

• We have recently opened a phase 2 trial, which includes newly-diagnosed DIPG patients (NCT04049565)
  - This trial will enroll 30 DIPG patients

• Some patients could possibly benefit from continued indoximod-based therapy after progression, using an adaptive management algorithm that has shown promise in non-DIPG patients with relapsed brain cancer:

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