**Abstract**

**PPTP in Vitro Testing Methods**

**Methods**

- In vitro testing was performed using IMC-A12 on a panel of cell lines (n=27) and solid tumor panels. In vitro testing was performed using culture medium supplemented with 20% FBS. It was tested against the PPTP in vitro panel at concentrations from 0.01 to 100 nM. Each cell line was tested in triplicate, and the mean fluorescence value was used to determine the antiproliferative effect. The cell line panel included IMC-A12 for pediatric solid tumors.

**Methods**

- The PPTP includes a molecularly characterized in vitro panel of cell lines representing most of the common types of childhood solid tumors and childhood ALL. IMC-A12 was tested against the PPTP in vitro panel at concentrations from 0.01 nM to 100 μM using culture medium supplemented with 20% FBS. It was tested against the PPTP in vitro panel at a dose of 1 mg per mouse administered twice weekly for six weeks via IP injection. IMC-A12 activity was determined from the percentage of viable cells using fluorescein diacetate (FDA)/propidium iodide (PI) staining and fluorescence-activated cell sorting (FACS).

**Results**

- IMC-A12 demonstrated significant antiproliferative activity against a range of pediatric solid tumors and childhood ALL.

**Conclusions**

- IMC-A12 demonstrated broad antiproliferative activity against PPTP in vitro solid tumor panels. Further studies characterizing molecular predictors of response, as well as the activity of combinations of IMC-A12 with other agents, are anticipated.

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**PPTP in Vivo Testing Methods**

**Methods**

- In vivo testing was performed using IMC-A12 on a panel of cell lines (n=27) and solid tumor panels. In vivo testing was performed using culture medium supplemented with 20% FBS. It was tested against the PPTP in vivo panel at concentrations from 0.01 nM to 100 μM. Each cell line was tested in triplicate, and the mean fluorescence value was used to determine the antiproliferative effect. The cell line panel included IMC-A12 for pediatric solid tumors.

**Results**

- IMC-A12 demonstrated limited activity against the PPTP in vivo panel, possibly due to the use of high serum concentrations. In vivo activity was greatest for Ewing sarcoma and rhabdomyosarcoma cell lines.

**Conclusions**

- IMC-A12 demonstrated broad growth inhibitory activity against the PPTP in vivo solid tumor panels. The greatest activity observed was against rhabdomyosarcoma xenografts with complete remission observed for Rh28.

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**Gene Expression for IG-1, IFG-2, IGF-1R, and IRB-1 (Affymetrix HG-U133 Plus 2.0 Arrays)**

- Gene expression analysis was performed using Affymetrix HG-U133 Plus 2.0 Arrays.

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**CONCLUSIONS**

- IMC-A12 demonstrated limited activity against the PPTP in vitro panel, possibly due to the use of high serum concentrations.

- IMC-A12 demonstrated broad growth inhibitory activity against the PPTP in vivo solid tumor panels. The greatest activity observed was against rhabdomyosarcoma xenografts with complete remission observed for Rh28.

- Most PPTP solid tumor xenografts and cell lines express IGF-1R at some level, but differ in their ligand expression: the rhabdomyosarcoma, Wilms, ependymoma, and neuroblastoma xenografts primarily express IGF-2 while the Ewing sarcoma expresses IGF-1.

- There is no clear correlation between expression of IGF-1R and its ligands and IMC-A12 in vitro and in vivo activity.

- IMC-A12 was provided to the PPTP by ImClone Systems. Supported by NCI NO1CM42216.