AO-176, a highly differentiated humanized anti-CD47 antibody, exhibits single-agent and combination anti-tumor efficacy with chemotherapy and targeted antibodies in pre-clinical models.

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**Abstract**

目的：鉴定一种单抗和组合治疗中化疗药物和靶向药物的抗肿瘤效果。

方法：我们研究了AO-176单抗和组合治疗中化疗药物和靶向药物的抗肿瘤效果。结果显示：AO-176单抗针对CD47/β1的结合具有直接杀伤作用。

结论：AO-176单抗和组合治疗中化疗药物和靶向药物的抗肿瘤效果。

**Figure 1**

- **AO-176 Displays a Unique Binding Pattern to CD47 on the Surface of Tumor and Normal Cells**
  - Figure A: Fluorescence micrographs showing the distinct binding pattern of AO-176 to discrete regions on the cell surface of tumors and normal cells (green). Figure B: Fluorescence microscopy images of AO-176 (red) binding to different cell types (red). Figure C: Knockout of integrin β1 leads to abolished AO-176 binding on tumor cells.

- **AO-176 Binds CD47 Complexed with Integrin β1: Negligible RBC Binding (Integrin β1 negative)**
  - Figure A: AO-176 binds CD47 complexed with integrin β1 negative RBCs, but not tumor cells (green). Figure B: Integrin β1 is detected in CD47+/ αPD-L1 using AO-176, not HO-176.

- **AO-176 Binds CD47 Complexed with Integrin β1: Negligible RBC Binding (Integrin β1 negative)**
  - Figure A: AO-176 binds CD47 complexed with integrin β1 negative RBCs, but not tumor cells (green).

- **AO-176 Binds CD47 Complexed with Integrin β1: Negligible RBC Binding (Integrin β1 negative)**
  - Figure A: AO-176 binds CD47 complexed with integrin β1 negative RBCs, but not tumor cells (green).

**Conclusions**

- AO-176 is the only clinical stage anti-CD47 antibody with direct killing activity. It is highly differentiated from current clinical agents targeting the CD47 axis.
  - AO-176 is the only anti-CD47 antibody to selectively bind CD47 complexed to integrin β1, allowing context-dependent preferential binding to tumors.
  - RBCs do not express integrin β1, explaining the negligible binding by AO-176.
  - AO-176 exhibits single-agent and combination efficacy with chemotherapy and targeted antibodies.
  - AO-176 is currently being evaluated in a Phase 1 clinical trial (NCT03839486) for the treatment of patients with select solid tumors.