

Use of SGN35 or brentuximab vedotin in anaplastic large-cell lymphoma: a case report in paediatrics



BACKGROUND

- ✓ Lymphoma is one of the most frequent hemopathy among children and young adults.
- ✓ Anaplastic large cell lymphoma (ALCL) affects 15% of these hemopathic children under 15 years old and 40% above 15 years old in France.

CD30 has been identified as an excellent therapeutic target in lymphomas that express CD30, which is a member of the tumor necrosis factor receptor (TNFR) superfamily. CD30 is uniquely expressed in classical Hodgkin lymphoma and ALCL and normal activated T, B and natural killer cells but is not expressed in normal tissues.

Over the past 20 years, monoclonal antibodies (mAbs) have emerged as a new and important focus for cancer therapeutics

Brentuximab vedotin or SGN35 is a monoclonal antibody-drug conjugate (mADC) composed of four components (Figure 1) :

- ✓ The anti-CD30 monoclonal chimeric antibody (mAb) IgG1
- ✓ An attachment group
- ✓ A protease-cleavable linker that covalently attaches monomethylauristatin E (MMAE) to mAb
- ✓ The potent microtubule polymerization inhibitor MMAE

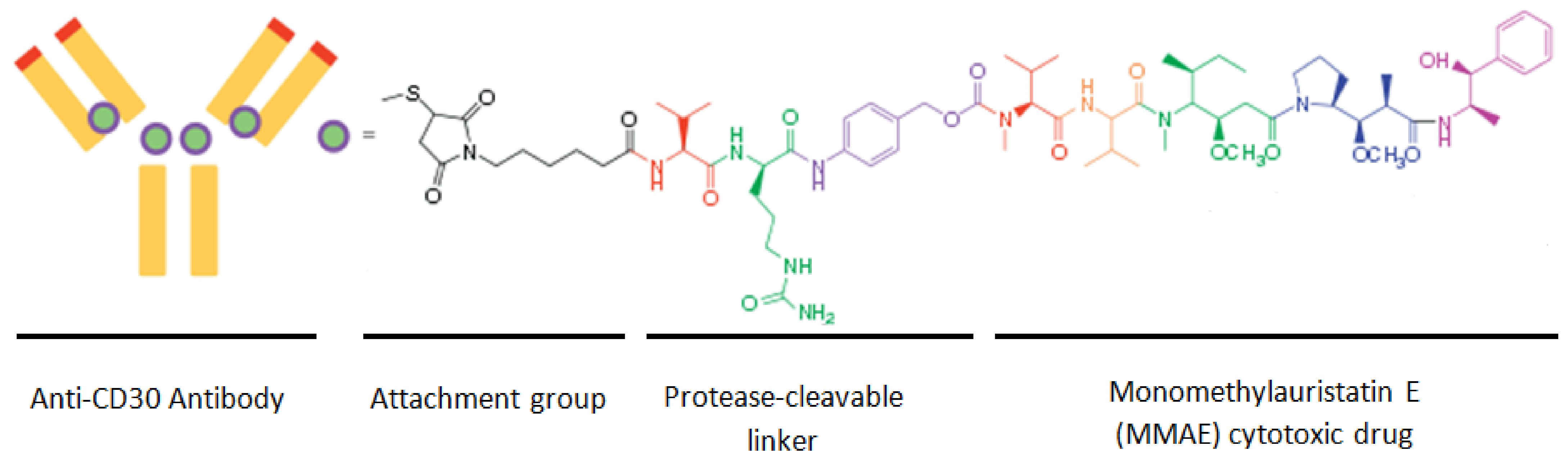


Figure 1 : Structure of brentuximab vedotin or SGN35 (d'après 1)

Brentuximab vedotin undergoes internalization into and releases MMAE which binds tubulin and prevents polymerization and cell growth.

MMAE leads to apoptotic cell death.

Brentuximab vedotin activity is established in the Hodgkin lymphoma and relapsed or refractory systemic ALCL CD30+.

OBJECTIVE

The aim of this work was to report the use of brentuximab vedotin in a pediatric case.

METHODS

- A literature search was undertaken about the use of brentuximab vedotin in pediatrics.
- Administrative work has been performed to obtain the treatment for the patient.

RESULTS

In July 2012, FDA licensed this mADC to treat CD30+ Hodgkin lymphoma and relapsed or refractory systemic ALCL in adults and the EMA licensed this mADC in October 2012. Nevertheless, brentuximab vedotin is still delivered with a temporary authorization for use (until March probably).

A Phase I/II study in pediatrics is at the moment recruiting. Brentuximab vedotin is administered every three weeks at 1,8mg/kg dose (half-life ranged from 4 to 6 days and steady-state was achieved in 21 days for the ADC).

CONCLUSION

After the 4th dose of brentuximab vedotin, treatment was well tolerated by the patient and tumour regression has been observed. Among adults, the median of response is about 12 months. Thus, confirmation of efficacy still has to be evaluated. Further studies are required to establish the efficacy and safety profile in paediatric population.

Case Report

June 2012

A 8 years old male child, with diagnosis of ALCL, was treated according to the ALCL99 protocol.

August 2012

Two months after diagnosis, tumour grew under this first line chemotherapy.

A pluridisciplinary committee decided to start a treatment by brentuximab vedotin.

A total of 5 cures spaced of 3 weeks combined with chemotherapy has been scheduled. Tumourous syndrome disappeared, thorax imagery normalized, fever and pulmonary and mediastinum adenopathies decreased.