Accelerated Pathway from Antibody to ADC

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Landscape of Clinical Antibody-Drug Conjugates

- **66%**
  - 217 - Clinically Active

- **4%**
  - 14 - Approved

- **30%**
  - 100 - Discontinued & Clinically Not Active

Source: *Beacon* Intelligence Database, October 2023
## Discontinued & Not Active ADCs (Clinical)

<table>
<thead>
<tr>
<th>Payload Class</th>
<th>Tubulin Inhibitors</th>
<th>DNA Damaging agents</th>
<th>Topoisomerase inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commonly used payloads</td>
<td>Auristatin (MMAE, MMAF), Maytansine (DM4, DM1), Tubulysin (AZ13599185)</td>
<td>Duocarmycin (DUBA), Indolino-benzodiazepine (IGN), Pyrrolobenzodiazepine (PBD)</td>
<td>SN-38, DXd/ DX8951, Camptotheacin, Doxorubicin</td>
</tr>
<tr>
<td>Discontinued ADCs (Discontinued after PI, PII or PIII)</td>
<td>62</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>Developers</td>
<td>Mersana Therapeutics, Bayer, Amgen, ImmunoGen, Boehringer Ingelheim</td>
<td>Seagen, Roche-Genentech, Pfizer, Celltech Therapeutics, Bristol Myers Squibb</td>
<td>Daiichi Sankyo, Seagen, Immunomedics</td>
</tr>
</tbody>
</table>

Source: Beacon Intelligence Database, October 2023
Is this an **ADC Target**?

Do you have right **Payload linker**?
DAR conventional

Kadcyla_intact

Kadcyla_in house

DAR 3.4

DAR 3.5
Biodistribution: the ADC cQA
Multi-Attribute Mapping (MAM)

- Oxidation?
- Deamidation?
- Glycation?

< specification?

proteolysis

LC-MSMS

batch release
SiteDAR

Drugs at same sites?

In the same amounts?

proteolysis

LC-MSMS

VVSVLTVLHQDWLNGKEYK

[DM1]
ADC sample mAb sample

Which site? How much?

VVSLTVLHQDWLNGKEYK

ADC sample mAb sample

VVSLTVLHQDWLNGKEYK

ADC sample mAb sample
mAb modified at antigen site
Diastereomers!
At different ratios
Measurement reproducible of SiteDAR

Commercial Kadcyla replicates
Same DAR – different sites

Commercial Kadcyla vs In-House Kadcyla
ADC biodistribution by design

Conceive

Conjugate

Characterize
Center for NMR Excellence
NMR Can Help Answer How Does Conjugation Change 3D Ab Structure

Herceptin (Native)
Herceptin-NEM (Capped)
Herceptin-DXD (Linker Payload)

https://doi.org/10.2210/pdb1IGT/pdb
Methyl Groups Present in Amino Acids

Alanine
Valine
Leucine
Isoleucine
Methionine
Threonine

(37) (60) (48) (15) (6) (55)

(221) Methyl-group containing amino acids in Trastuzumab
HSQC as A Method To Visualize Methyl Groups
HSQC of Herceptin
HSQC of Herceptin-NEM
Overlay of **Herceptin** with **Herceptin-NEM**
HSQC of **Herceptin-DXD**

**Herceptin-DXD**

**Herceptin-DXD (Linker Payload)**

**Deruxtecan (DXD)**
Overlay of **Herceptin** with **Herceptin-DXD**
Overlay of Herceptin-NEM with Herceptin-DXD
NJ Bio, Inc.

Best Contract Research (CRO) Provider Winner

Runner Up 2020
Best Contract Research (CRO) Provider

NJ Bio
2021

2022