NOVEL CELL-TYPE THERAPEUTIC PLATFORMS IN ONCOLOGY: IF YOU’VE SEEN ONE, YOU’VE SEEN...ONE
Cello Health BioConsulting's Insight Series Webinar

August 11th, 2020
Cello Health BioConsulting: Who We Are

- Cello Health BioConsulting is a knowledge-based consultancy deeply rooted in science; we often evaluate early stage programs before much, if any, clinical data is available. In the biopharma world, we are known for our “unconventional insight” – forward thinking, independent, objective strategic advice across all therapeutic areas.

- Cello Health BioConsulting provides strategic advice for corporate growth and partnering strategies, disease area selection, indication prioritization, opportunity search and evaluation, opportunity and landscape assessment, valuation and forecasting, early market access strategy and early value profile development.

- Cello Health BioConsulting has a strong and broad network of leaders and influencers across biotech and pharma, which provides a deep understanding of next wave issues, the competitive and market landscapes, and keeps us well-informed and ahead of industry trends.

- Visit our website at www.cellohealthbioconsulting.com
Proliferation of Novel Cell Type Platforms in the Oncology Competitive Landscape – PART 1

Introduction

An increasing number of companies believe that engineering alone will be an insufficient substitute for biological properties honed over millions of years within different cell types.

There is little if any debate among the scientific community about the importance of immune cells in fighting cancer and keeping it at bay. The billion-plus dollar question instead revolves around how to unleash or augment its capacity to do so. Perhaps more so than any other modality to date, cancer cell therapies have captured the imaginations and wherewithal of industry, investor, and oncologist communities alike for their perceived ability to drive a robust and tailored antitumor immune response across varied oncology settings.

A fundamental but often vaguely understood component of cell therapy platforms is the cell itself. The endogenous immune system is in fact a patchwork of different cell types, each with different means and ways.

Webinar Participants

Novel Cell-Type Therapeutic Platforms in Oncology: If You’ve Seen One, You’ve Seen...One

Moderator:

Joel Sandler, PhD
Principal and Practice Head
Cello Health BioConsulting

Panelists:

Lawrence Lamb, PhD
EVP and CSO
Incysus Therapeutics

Kurt Gunter, MD
CMO
Kuur Therapeutics
Strategy is Critical to Achieving Optimal Positioning, Value Inflection, and Partnering/Commercial Success in Dynamic ACT Field

Unprecedented/undisclosed competition (IP = knowhow)
Technical barriers, clinical risk
Generic, doggedly effective SoC
Mounting access hurdles, out-of-pocket expenses

Optimal Strategy is a Critical Component to Achieving Maximum Value Inflection

ACT Sector: Headwinds and Tailwinds
Translation of amazing science
Tremendous influx of capital
Company formation, proliferation
Demand for durable remissions
Potentially rapid signal generation

Market Cap
Time
Valuation Driven by Clinical Data
Valuation Driven by Data + Strategy
Venture Dollars Raised for Cell Therapy

Venture Dollars (Gene/Cell therapy)

2017  2018  2019  2020 (YTD*)

BCIQ, CHBC analytics; *as of April 1st, 2020
ACT Sector Driven to Expand Beyond First Approvals With Improved Options in B-Cell Malignancies, Penetration Into Additional Heme and Solid Tumors, and ‘One-Pot’ Solutions

Evaluate Ltd.; CHBC analysis; CPIs: Checkpoint Inhibitors, ACTs: Adoptive Cell Therapies
Allogeneic ACT Positioned as a More Convenient, Cost-effective Version of Auto, or Something New Altogether?

<table>
<thead>
<tr>
<th>Safety, Simplicity</th>
<th>Allo CARs?</th>
<th>Efficacy, Complexity, Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Naked’ mAbs</td>
<td>ADCs</td>
<td>Bispecific Antibodies</td>
</tr>
<tr>
<td>• Off-the-shelf</td>
<td>• Targeted toxin payload delivery</td>
<td>• Off-the-shelf</td>
</tr>
<tr>
<td>• Benign safety</td>
<td>• Reasonably safe, well-tolerated</td>
<td>• T-cell redirecting</td>
</tr>
<tr>
<td>• Chronic management</td>
<td>• On-target + bystander effect</td>
<td>• Active in cell tx failures</td>
</tr>
<tr>
<td>• Combinable</td>
<td>• Active in chemo, mAb failures</td>
<td>• Controlled induction vs. cell tx</td>
</tr>
<tr>
<td>• Modest ORR</td>
<td>• Limited role of host immunity</td>
<td>• Toxicity concerns</td>
</tr>
<tr>
<td>• Rarely durable</td>
<td>• Many variables (linker, payload, drug-antibody ratios)</td>
<td>• Less durable vs. CARTs</td>
</tr>
<tr>
<td>• biobetters, generic competition</td>
<td>• Combo or monotherapy</td>
<td>• Limited multiplexing capacity</td>
</tr>
<tr>
<td>• Combo or monotherapy</td>
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</tr>
<tr>
<td>• early, adjuvant, maintenance</td>
<td>• Salvage settings</td>
<td>• Late or early-stage (if safe)</td>
</tr>
</tbody>
</table>

Strengths/Opportunities | Weaknesses/Threats | Positioning

CHBC insight
T-Cells and NKs Dominant the Allogenic Pipeline; Small No. of Programs Involving Rarer Cell Types ($\gamma\delta$ T-cells, NK/Ts)

Cell Therapy Programs (n=668)*

- Auto: 60%
- Undefined: 26%
- Allo: 14%

Allogeneic Subset (n=96)

- T-cell: 44
- NK: 31
- NK/T: 5
- CIK: 3
- Gamma-delta: 2
- PBMC: 1
- Stem cell: 10

*from CHBC's Adoptive Cell Therapy (ACT) Pipeline database; data pulled in March 2020; includes preclinical- and clinical-stage assets worldwide; secondary sources include AdisInsight and Cortellis
Novel Cell Types Have Respective Advantages and Disadvantages

<table>
<thead>
<tr>
<th></th>
<th>Allo Without Editing</th>
<th>GvHD</th>
<th>Durability</th>
<th>Solid Tumor Penetration</th>
<th># of Assets in Development</th>
<th>Immune Stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-cell</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>High 712 WW</td>
<td>High</td>
</tr>
<tr>
<td>Natural Killer (NK)</td>
<td>High (Limited need for extensive editing)</td>
<td>Low (Lack of TCR and MHC restrictions)</td>
<td>Low (Lack of long-term in vivo persistence)</td>
<td>Med</td>
<td>High 80 WW</td>
<td>Med</td>
</tr>
<tr>
<td>Macrophage (MΦ)</td>
<td>Med</td>
<td>?</td>
<td>?</td>
<td>High (Modulate solid tumor TME)</td>
<td>Low 4 WW</td>
<td>Med (Activate adaptive immune response by presenting tumor material)</td>
</tr>
<tr>
<td>Natural Killer T Cells (NKT)</td>
<td>Med</td>
<td>Low</td>
<td>?</td>
<td>Med</td>
<td>Low 7 WW</td>
<td>?</td>
</tr>
<tr>
<td>γδ T-cells</td>
<td>High</td>
<td>Low</td>
<td>?</td>
<td>Med</td>
<td>Med 19 WW</td>
<td>?</td>
</tr>
</tbody>
</table>

*High/Medium/Low qualities rated by desirability using colors shown.

CHBC insight, ACT database
## Allogeneic Cell Sources Have Respective Advantages and Disadvantages

<table>
<thead>
<tr>
<th>Different cell types</th>
<th>Scalable</th>
<th>Clonally Pure</th>
<th>GvHD Risk</th>
<th>Host Rejection</th>
<th>Teratoma Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>iPSC</strong></td>
<td>High</td>
<td>High</td>
<td>Med</td>
<td>Med</td>
<td>Med</td>
</tr>
<tr>
<td>High Can differentiate into any human cell type(^1).</td>
<td>High Unlimited ability to self-renew and can be used indefinitely(^2).</td>
<td>High Homogenous; generated from one cell line(^2).</td>
<td>Med HLA disparity between effector cells and host can cause GvHD(^1).</td>
<td>Med HLA disparity also causes host immune response(^3).</td>
<td>Med Pluripotency of iPSCs carries risk of tumor development(^6).</td>
</tr>
<tr>
<td><strong>Umbilical cord blood (UCB)</strong></td>
<td>Med Rich source of naïve T cells and stem cells that can be differentiated(^3).</td>
<td>Med Stem cells can be expanded ex-vivo, but large-scale manufacturing optimization is still a challenge(^3).</td>
<td>Low Heterogenous mix of cells; selected cell type must be purified out(^4).</td>
<td>Low Cells have unique Ag-naïve status and impaired NFAT signaling(^2).</td>
<td>Low Cells not pluripotent so do not form teratomas.</td>
</tr>
<tr>
<td><strong>Healthy Donor</strong></td>
<td>Low Whole blood contains PBMCs and a relatively low conc. of HSCs.</td>
<td>Low Continuous donations needed to create bank of different HLA types(^3).</td>
<td>Low Heterogenous mix of cells; selected cell type must be purified out(^4).</td>
<td>Med HLA disparity can cause GvH response(^2).</td>
<td>Low Cells not pluripotent so do not form teratomas.</td>
</tr>
</tbody>
</table>

\(^1\) Nianias, A. et al. (2019); \(^2\) Depil, S. et al. (2020); \(^3\) Presti, V.L. et al. (2018); \(^4\) Dolstra, H. et al. (2017); \(^5\) Graham, C. et al. (2018); \(^6\) Duinsbergen, et al. (2009)

*High/Medium/Low qualities rated by desirability using colors shown.*
Thank you for attending the webinar **Novel Cell-Type Therapeutic Platforms in Oncology: If You’ve Seen One, You’ve Seen...One**; and please download our related white paper from cellohealthbioconsulting.com