2007: Seminal Workshop by NCI, NIH, FDA to Rank Immunotherapy Molecules with the Potential to Cure Cancer

Ranked #1

Twenty Years in the Making

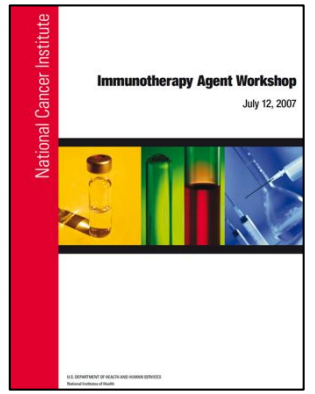
Approved in Bladder (33 Countries) and Lung Cancer (Saudi, SFDA)

Ranked #2

40+ Approvals by 2025
Many Single-Arm Trials
Micro-Satellite Stable Across Multiple Tumor Types

Table 1. Final Rankings of Agents with High Potential for Use in Treating Cancer

Rank*	Agent	Agent Category
1	IL-15	T-Cell Growth Factor
2	Anti-Programmed Death-1 (PD1)and/or anti–B7-H1 (PD1 Ligand)	**T-Cell Checkpoint Blockade Inhibitor
3	IL-12	Vaccine Adjuvant
4	Anti-CD40 and/or CD40L	Antigen Presenting Cell Stimulator
5	IL-7	T-Cell Growth Factor
6	CpG	Vaccine Adjuvant
7	1-Methyl Tryptophan	Enzyme Inhibitor
8	Anti-CD137 (anti–4-1BB)	T-Cell Stimulator
9	Anti–TGF-beta	Signaling Inhibitor
10	Anti–IL-10 Receptor or Anti–IL-10	Suppression Inhibitor
11	Flt3L	Dendritic Cell Growth Factor/ Vaccine Adjuvant
12	Anti-Glucocorticoid-Induced TNF Receptor (GITR)	T-cell Stimulator
13	CCL21 Adenovirus	T-Cell Attracting Chemokine
14	Monophosphoryl Lipid A (MPL)	Vaccine Adjuvant
15	Poly I:C and/or Poly ICLC	Vaccine Adjuvant
16	Anti-OX40	T-Cell Stimulator
17	Anti–B7-H4	T-Cell Checkpoint Blockade Inhibitor
18	Resiquimod and/or 852A	Vaccine Adjuvant
19	LIGHT and/or LIGHT vector	T-Cell Stimulator
20	Anti–Lymphocyte Activation Gene-3 (LAG-3)	T-Cell Checkpoint Blockade Inhibitor



National Cancer Institute

Immunotherapy Agent Workshop

July 12, 2007

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

NATIONAL CANCER INSTITUTE
IMMUNOTHERAPY AGENT WORKSHOP
JULY 12TH, 2007

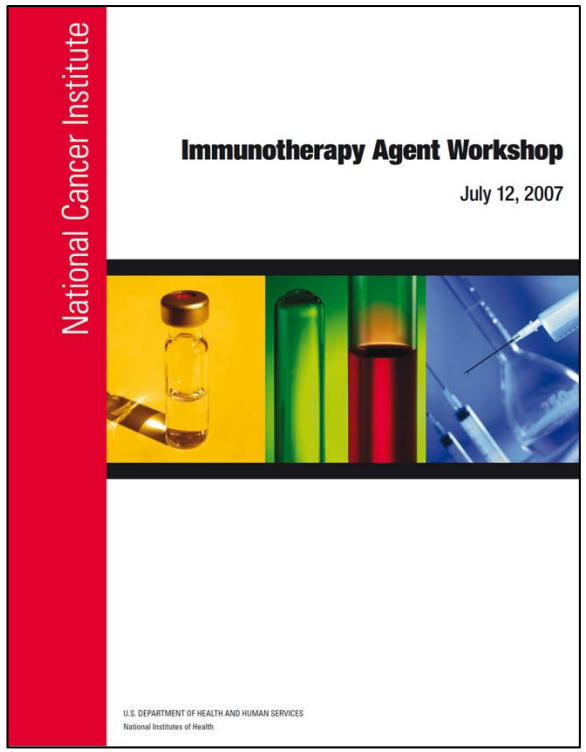
EXECUTIVE SUMMARY

There is an ongoing explosion of knowledge in the immunological sciences with the discovery of many agents that have the potential to serve as immunotherapeutic drugs. For a variety of reasons, few of these are being tested in humans. The workshop developed a ranked list of agents with high potential for use in treating cancer. Despite substantial demonstrated immunological efficacy, these agents are not broadly available for testing in patients with cancer. The ranking by workshop participants was based on the likelihood for efficacy in cancer therapy and was exceedingly well-vetted, with broad and substantial input. The exceedingly broad nature of the consensus behind this list will facilitate subsequent NCI discussions on the availability of clinical grade immunotherapeutic drugs for human trials and will inform other governmental agencies, nongovernmental funding agencies, industry, and individual investigators that these agents have broad appeal to the immunotherapy community and, by consensus, hold particular promise for use in cancer therapy.

Twenty agents are presented on the list, presented in rank order. However, all are considered to have substantial potential for cancer therapy. Criteria essential for inclusion on the list included:

- Potential for use in cancer therapy.
- Perceived need by multiple, independent clinical investigators.
- Potential use in more than one clinical setting (i.e., against different tumor types or as part of multiple therapy regimens).
- Not broadly available for testing in patients.
- Not commercially available or likely to be approved for commercial use in the near future.

The 20 agents were selected from a list of 124 agents suggested to an NCI Web site asking for suggestions and advice about "agents with known substantial immunologic or physiologic activity that have not been tested or have been inadequately tested in cancer patients." The Web site was publicized widely by the NCI with requests for advice sent to grantees with immunology or immunotherapy grants and to prior recipients of RAID awards, as well as to intramural scientists involved in immunology or immunotherapy. The Web site was further publicized to the membership of the major scientific societies involved in immunology, immunotherapy and cancer research, namely the American Association for Cancer Research (AACR), American Association of Immunologists (AAI), American Society of Oncology (ASCO), American Society of Hematology (ASH), the Cancer Vaccine Consortium (CVC), and the International Society of Biological Therapy (iSBT).



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*Final rank was derived from voting by the workshop participants. The agents are listed according to median rankings. Means were used to break ties (see Table 4 for details).
**Anti-CTLA-4, a T-cell checkpoint blockade inhibitor, was considered of exceedingly high value but was not included on the list, as it is being produced by Bristol-Myers Squibb and Pfizer and is likely to be approved by the FDA within the foreseeable future.

In all, 124 agents were suggested via the Web site. Respondents expressed particular interest in vaccine adjuvants; T-cell growth factors; agents to inhibit immune checkpoint blockade; functional antibodies, cytokines, ligands, and receptors; and agents "left on the shelf" by drug companies, as well as suggestions for specific antigens for vaccines and antigen-specific antibodies.

The organizing committee[2] winnowed the list of 124 agents down to 30. The committee's focus was on agents with the greatest potential for multiple uses by multiple investigators supporting the development of multiple types of regimens, thereby excluding specific antigens for vaccines and antigen-specific antibodies desired by individual groups, regardless of their attractiveness or potential utility.

The organizing committee established the following criteria for the workshop participants to use as they assigned priorities to the agents under consideration:

- Potential for use in cancer therapy.
- Perceived need by multiple, independent clinical investigators.
- Potential use in more than one clinical setting (i.e., against different tumor types or as part of multiple therapy regimens).
- Not broadly available for testing in patients.
- Not commercially available or likely to be approved for commercial use in the near future.