

Immunotherapy Clinical Trials

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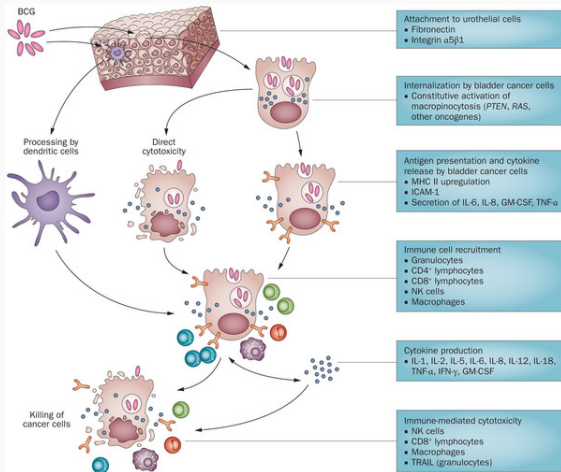
Idea: Use body's immune system to recognize and kill cancer cells

Not a new idea, but there are some high-profile newer drugs in this class

Examples of immunotherapies in oncology:

Cancer vaccines

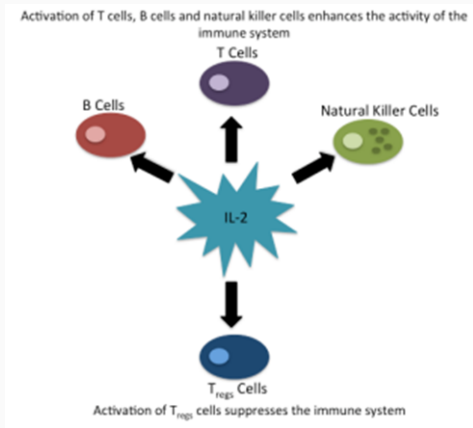
Example: BCG in bladder cancer



Examples of immunotherapies in oncology:

Cytokines

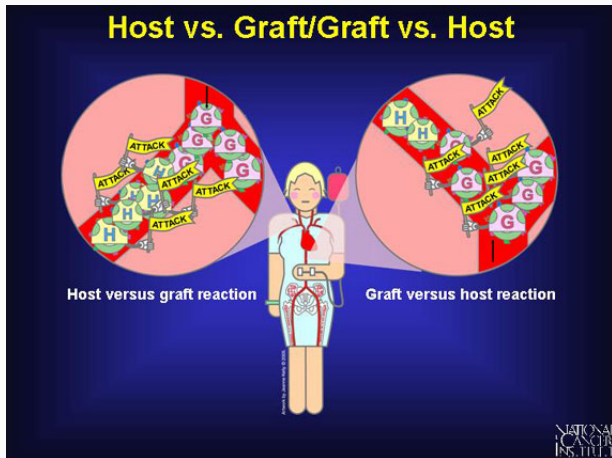
Example: IL-2 in melanoma and renal carcinoma; Interferon in melanoma and some hematologic malignancies



Examples of immunotherapies in oncology:

Allogeneic transplant

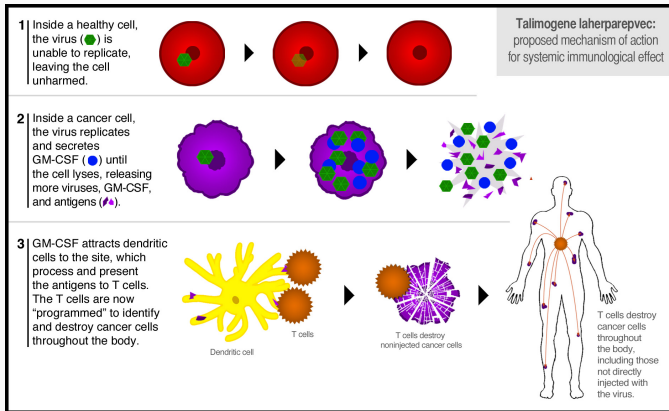
Example: Leukemias



Examples of immunotherapies in oncology:

Oncolytic viruses

Example: T-vec in melanoma

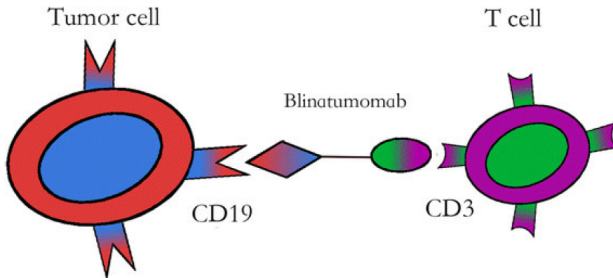


Examples of immunotherapies in oncology:

Monoclonal antibodies

Examples: trastuzumab in breast cancer (HER2), alemtuzumab in CLL (CD52), rituximab in non-Hodgkin's lymphoma (CD20), cetuximab (colorectal carcinoma), blinatumomab for ALL, CTLA-4 and PDL1 therapies for melanoma and other cancers

Figure Mechanism of Action for Blinatumomab



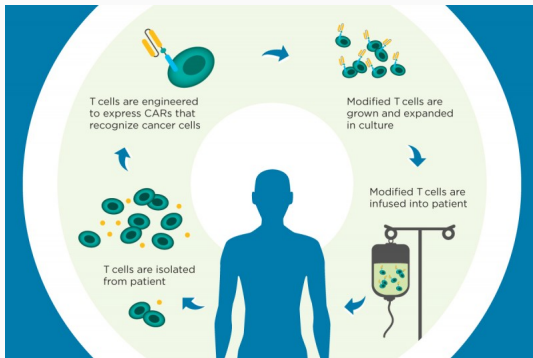
One arm of blinatumomab binds to CD3, the other binds to CD19. This binding engages the unstimulated T cells, which destroy the CD19-positive cells.³

Reprinted with permission from Wu J, Fu J, Zhang M, Liu D. Blinatumomab: a bispecific T cell engager (BiTE) antibody against

Examples of immunotherapies in oncology:

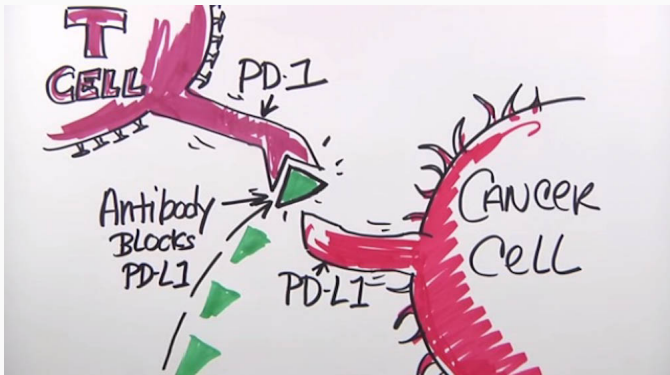
CAR T-cell therapy

Example: leukemia and lymphoma



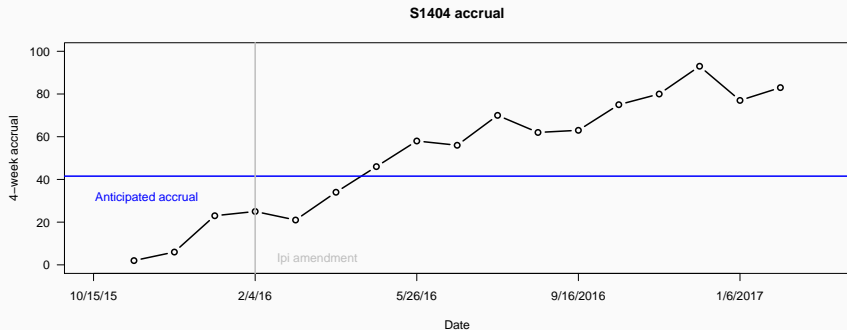
Examples of immunotherapies in oncology: Checkpoint inhibitors

Example: CTLA-4 and PDL1 drugs for a variety of cancers

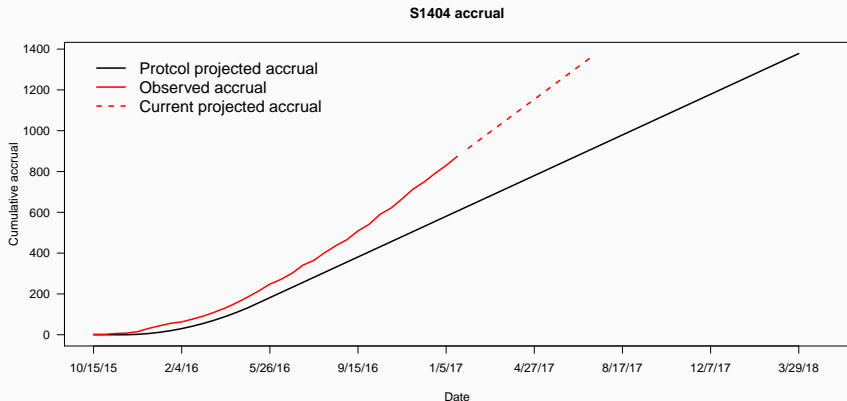


- Adjuvant therapy for advanced melanoma
- Control arm: Patient/physician choice of High-dose Interferon (cytokine therapy) or Ipilimumab (CTLA-4 therapy)
- Experimental arm: Pembrolizumab (PDL1 therapy)
- FDA registration trial

S1404 accrual



S1404 accrual implications



First interim/RFS analysis was planned for Fall 2019, now is expected **Fall 2018**.

If pembrolizumab is strongly positive at the first interim/RFS analysis:

- Merck will take the trial results to the FDA and European Health Authorities
- SWOG will have to provide all that data to Merck
- SWOG sites can and will be audited by the FDA

Because S1404 is an **FDA registration trial**, we need:

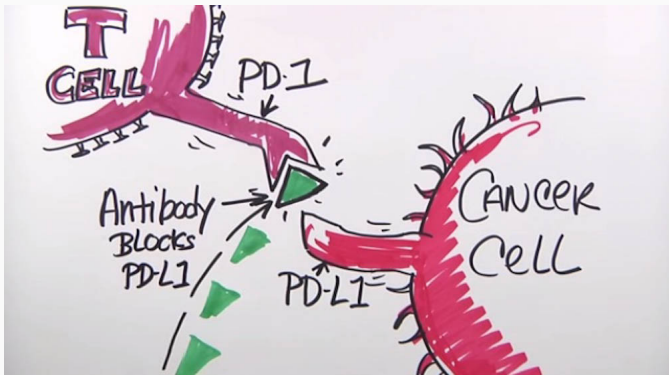
- More data than usual
 - especially detailed AE data
- No missing data
 - even if a test wasn't done, we need to document why it wasn't done and so why it is missing
- All of the scans done
 - scan images have to be uploaded through Triad into Rave
- QOL data
 - Some European countries require QOL data

S1404 and PDL1 data

Because S1404 is a FDA registration trial, we need **PDL1 status on all patients randomized.**

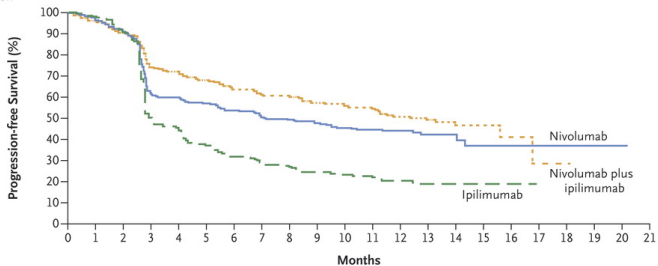
Specimen Submission Tally	N (%)
One submission	805 (87%)
Two submissions	115 (12%)
Three submissions	7 (1%)
Four submissions	2 (<1%)

Why we care about PDL1



Marker stratification – ignoring PDL1

A Intention-to-Treat Population

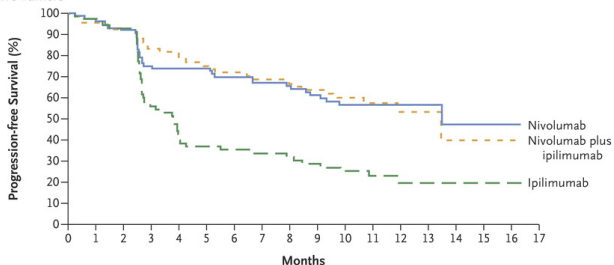


No. at Risk

Nivolumab	316	292	271	177	170	160	147	136	132	124	106	86	50	38	14	9	6	2	1	1	1	0
Nivolumab plus ipilimumab	314	293	275	219	208	191	173	164	163	151	137	116	65	54	18	11	7	2	1	0	0	0
Ipilimumab	315	285	265	137	118	95	77	68	63	54	47	42	24	17	7	4	3	0	0	0	0	0

Marker stratification – PDL1 positive

B Patients with PD-L1–Positive Tumors

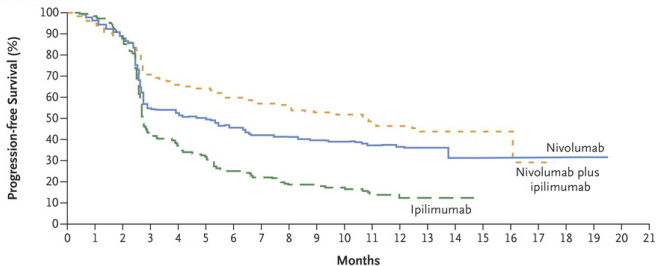


No. at Risk

Nivolumab	80	76	71	57	56	54	51	49	49	43	38	32	16	13	5	4	2	0
Nivolumab plus ipilimumab	68	63	61	53	52	47	44	42	42	39	34	24	16	12	3	1	1	0
Ipilimumab	75	69	66	40	33	24	22	21	21	17	16	15	9	6	3	2	2	0

Marker stratification – PDL1 negative

C Patients with PD-L1–Negative Tumors



No. at Risk

Nivolumab	208	192	178	108	105	98	88	80	76	74	63	50	31	24	9	5	4	2	1	1	1	0
Nivolumab plus ipilimumab	210	195	181	142	134	123	112	106	105	96	88	79	42	36	13	9	6	2	1	0		
Ipilimumab	202	183	166	82	72	59	44	39	35	31	26	22	12	8	3	1	0					

Questions?