

KEYTRUDA[®] (pembrolizumab)

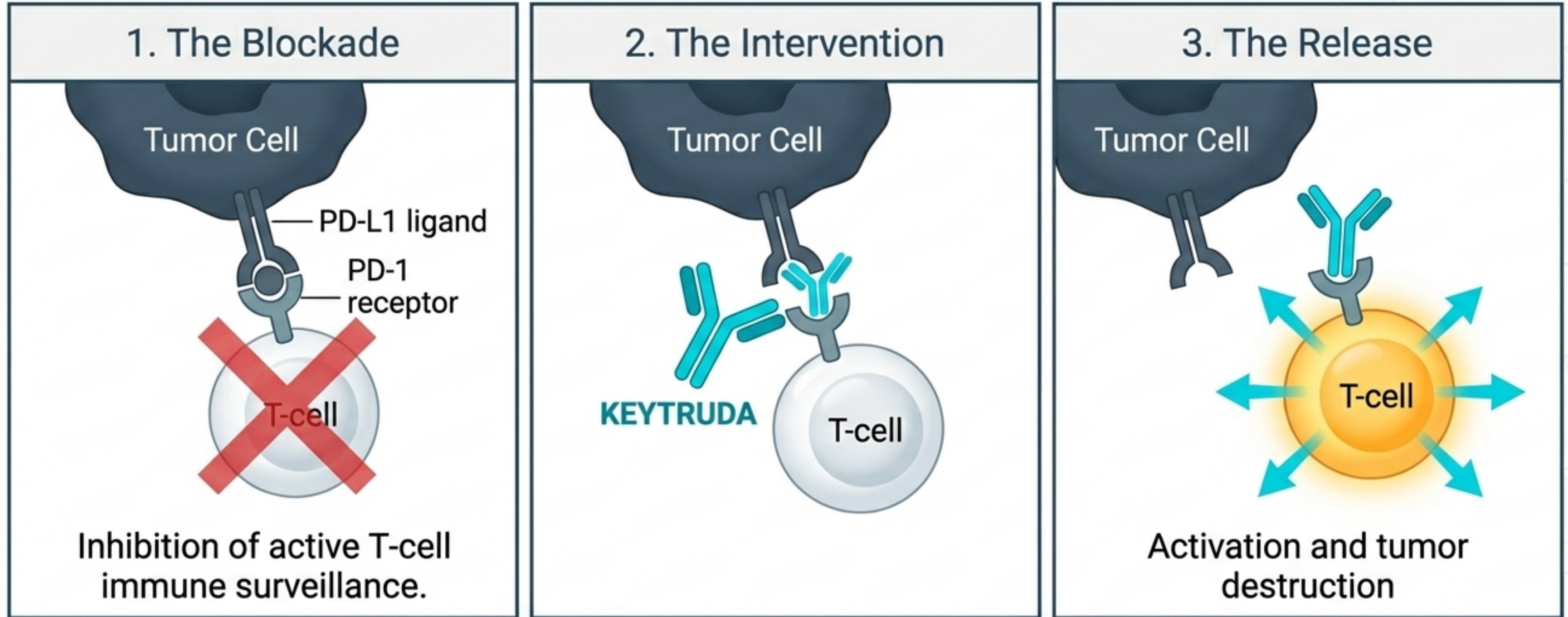
Clinical Prescribing Dashboard
& Efficacy Blueprint

Synthesis of indications, dosing, and pivotal trial data (Updated 05/2017)

THE MASTER INDICATIONS MATRIX

Disease State	Line of Therapy	Biomarker Requirement	Approval Basis
Melanoma	Any line	None	Regular
NSCLC (Monotherapy)	1 st -Line	PD-L1 TPS \geq 50% (No EGFR/ALK)	Regular
NSCLC (Monotherapy)	2 nd -Line+	PD-L1 TPS \geq 1%	Regular
NSCLC (Combination)	1 st -Line Nonsquamous	None	Accelerated
HNSCC	Post-Platinum	None	Accelerated
Classical Hodgkin Lymphoma	\geq 3 lines	None	Accelerated
Urothelial Carcinoma	Cisplatin-Ineligible OR Post-Platinum	None	Accelerated / Regular
MSI-H Cancer	Post-prior treatment	MSI-H or dMMR	Accelerated

Mechanism of Action: Releasing the Brakes



KEYTRUDA releases PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response.

Standard Dosing

200 mg

Intravenous infusion every 3 weeks.

Melanoma, NSCLC, HNSCC, Urothelial, and Adult cHL/MSI-H. Treat until disease progression, unacceptable toxicity, or up to 24 months.

Pediatric Exceptions

2 mg/kg

Up to a maximum of 200 mg every 3 weeks.

Pediatric cHL and Pediatric MSI-H cancers.

Administration Rules



Administer over 30 minutes.

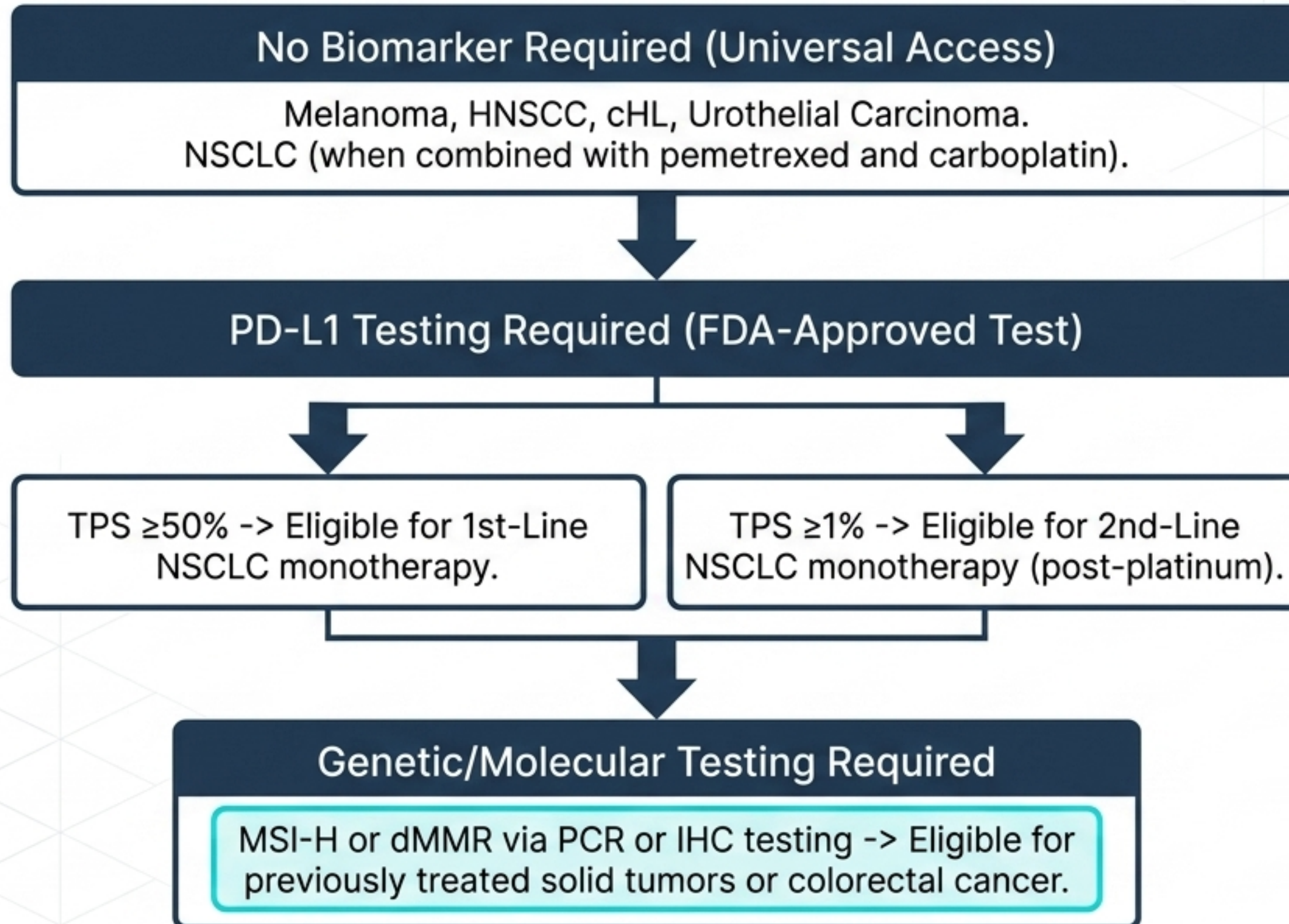


Use 0.2 to 5 micron in-line filter.

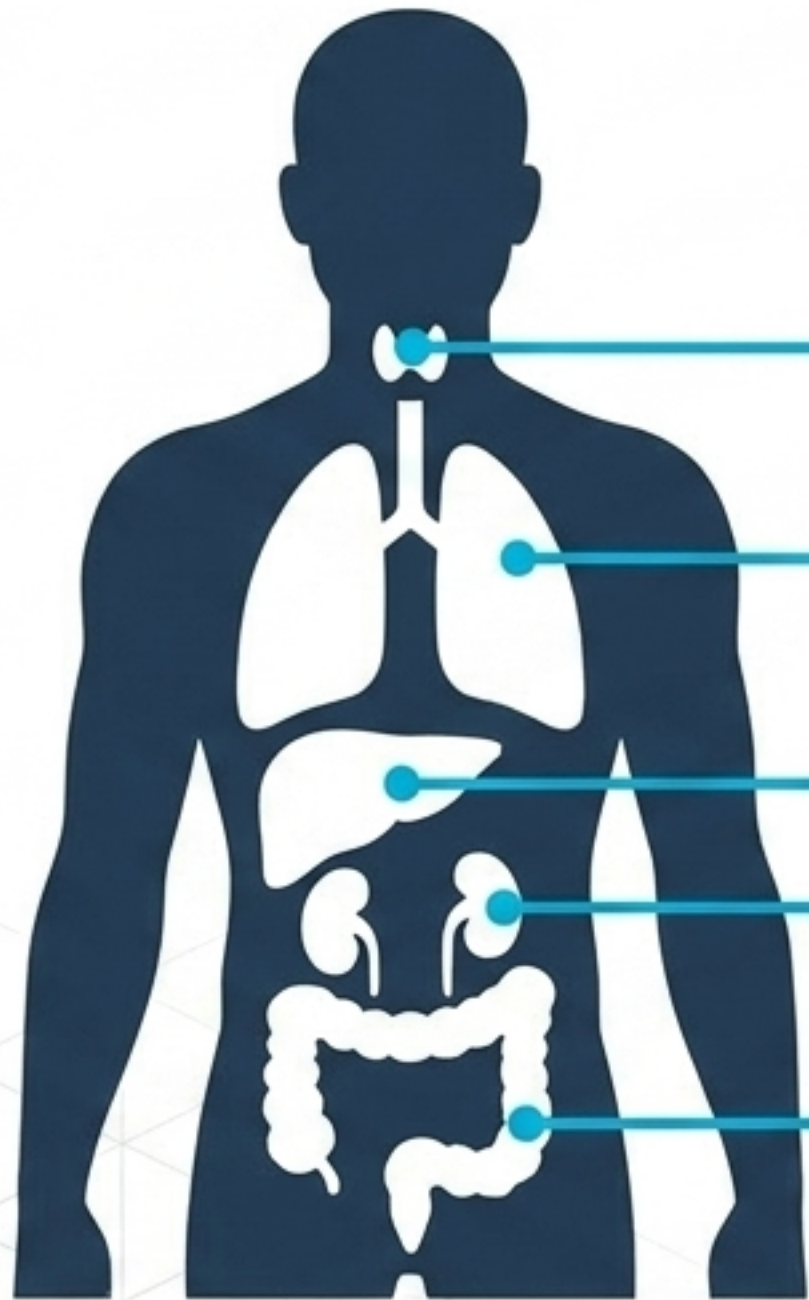


Dilute in 0.9% NaCl or 5% Dextrose (final concentration 1 to 10 mg/mL).

Precision Medicine Funnel: Biomarker Dependencies



Anatomical Safety Map: Immune-Mediated Toxicities



Endocrine Glands: Hypothyroidism (8.5%), Hyperthyroidism (3.4%), Hypophysitis (0.6%), Type 1 Diabetes (0.2%).

Lungs: Pneumonitis (3.4%). Highest risk with prior thoracic radiation.

Liver: Hepatitis (0.7%). Monitor for liver enzyme elevations.

Kidneys: Nephritis (0.3%).

Colon: Colitis (1.7%).

Embryofetal Toxicity: Can cause fetal harm. Advise highly effective contraception during and for 4 months post-treatment.

Toxicity Management: The Grade-to-Action Gauge

Moderate (Grade 2)

Severe/Life-Threatening
(Grade 3 or 4)

WITHHOLD KEYTRUDA

- Administer resume
- Administer corticosteroids (1 to 2 mg/kg/day prednisone)
- **Triggers:** Grade 2 pneumonitis, colitis, nephritis. AST/ALT >3 to 5x ULN.
- **Resolution:** Resume when adverse reaction recovers to Grade 0-1.

PERMANENTLY DISCONTINUE

- **Triggers:** Grade 3/4 pneumonitis/nephritis.
- AST/ALT >5x ULN.
- Grade 3/4 infusion reactions.
- Inability to reduce steroids to ≤ 10 mg/day within 12 weeks.

Exception: Endocrinopathies (Grade 3/4) often require withholding, not necessarily discontinuation, if controlled with hormone replacement.

Infusion-Related Reactions (0.2% incidence)

Timing:

Rapid onset (during or shortly after the 30-minute IV).

Symptoms:

Rigors, chills, wheezing, pruritus, flushing, hypoxemia.

Action:

Stop infusion and permanently discontinue for severe/life-threatening (Grade 3/4).

Immune-Mediated Reactions

Timing:

Delayed onset (median time to onset ranges from 1.3 months for hepatitis to 5.1 months for nephritis).

Symptoms:

Organ-specific inflammation (cough, diarrhea, jaundice, fatigue).

Action:

Corticosteroid intervention, withhold, or discontinue based on Grade.

Efficacy Dashboard 1: Melanoma

KEYNOTE-006 (Ipilimumab-Naive vs. Ipilimumab)

Overall Survival HR: 0.69 (Q3W) and 0.63 (Q2W)

PFS HR: 0.58

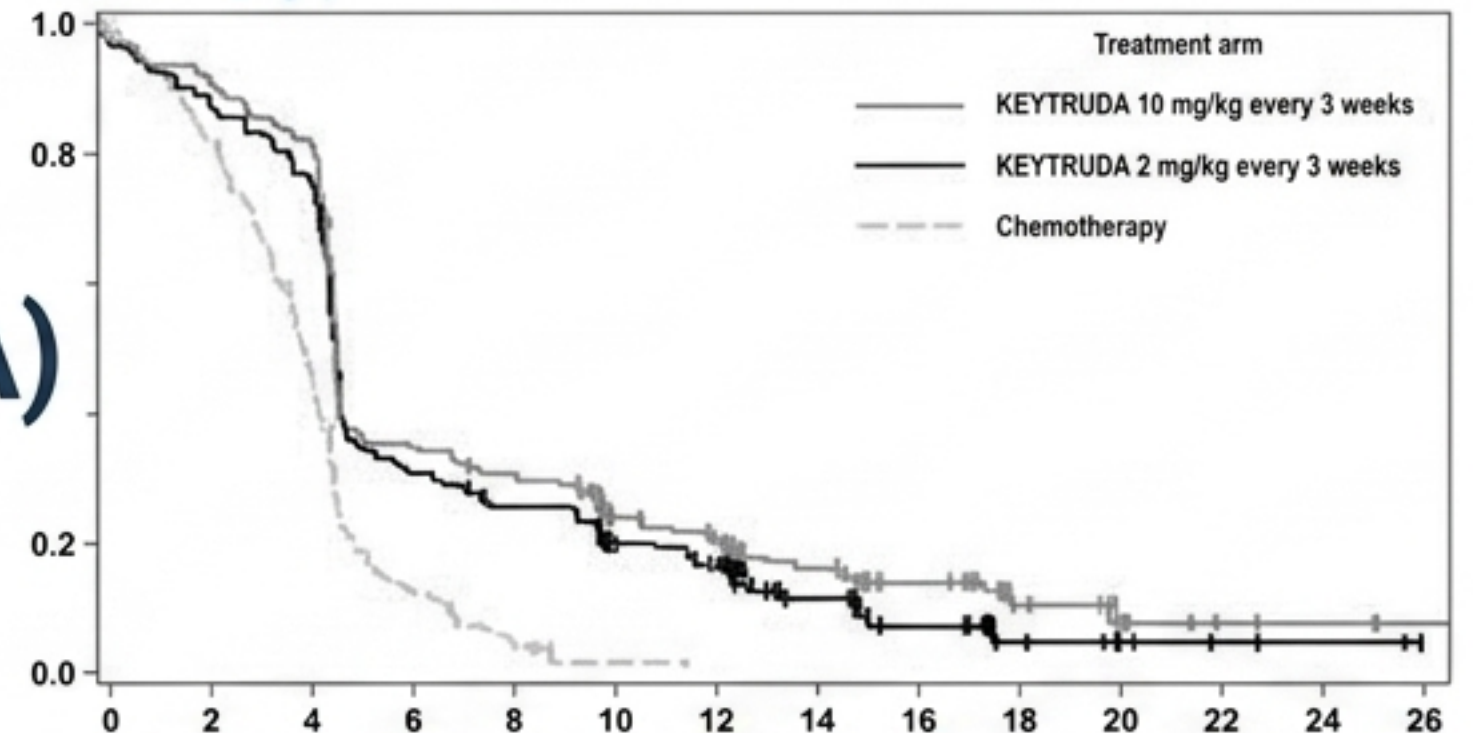
ORR: 33-34% (KEYTRUDA) vs. 12% (Ipi)

KEYNOTE-002 (Ipilimumab-Refractory vs. Chemotherapy)

PFS HR: 0.57 (2mg/kg) and 0.50 (10mg/kg)

ORR: 21-25% (KEYTRUDA)

vs. 4% (Chemo)



Efficacy Dashboard 2: NSCLC Monotherapy

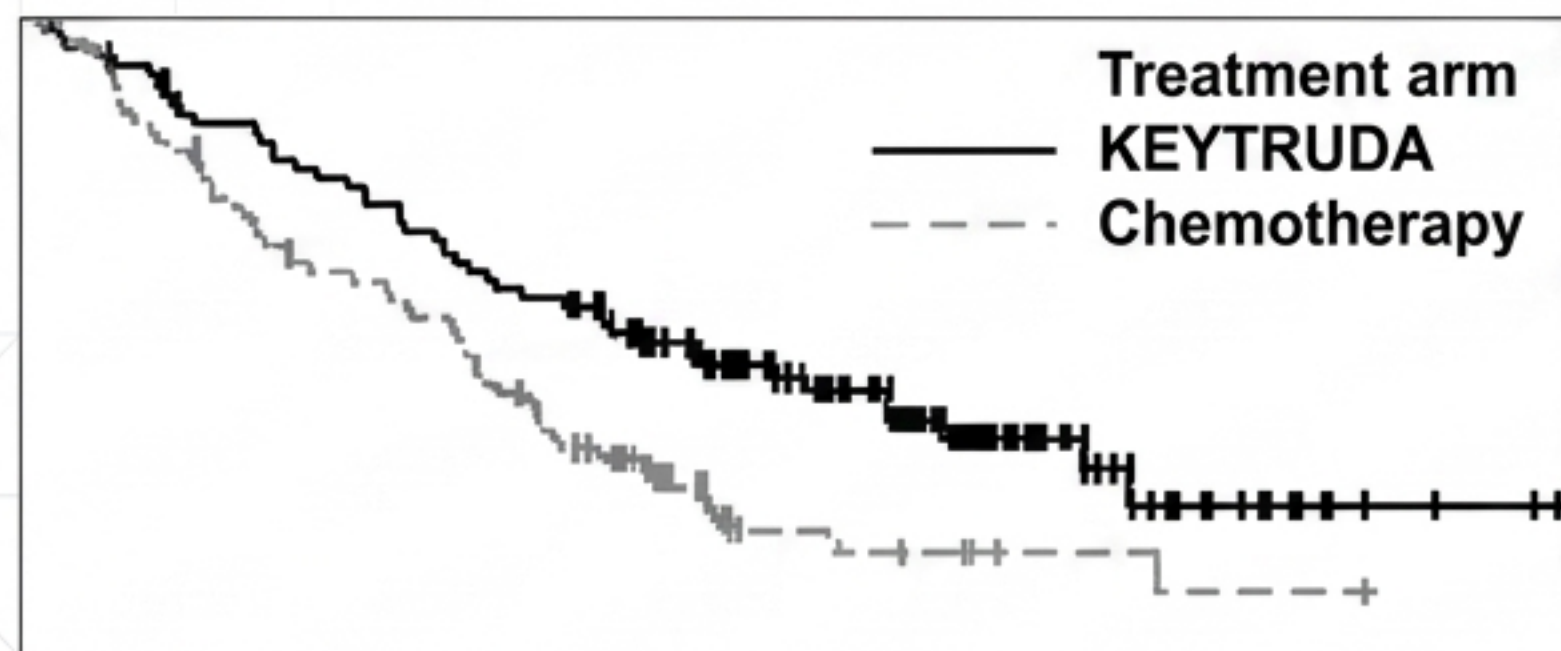
KEYNOTE-024 (1st-Line, TPS $\geq 50\%$)

Comparator: Platinum-containing chemotherapy.

ORR: **45%** (KEYTRUDA) vs. **28%** (Chemo)

PFS HR: **0.50**

OS HR: **0.60**



KEYNOTE-010 (Previously Treated)

Comparator: Docetaxel.

Subgroup TPS $\geq 50\%$:
OS HR **0.54/0.50**.

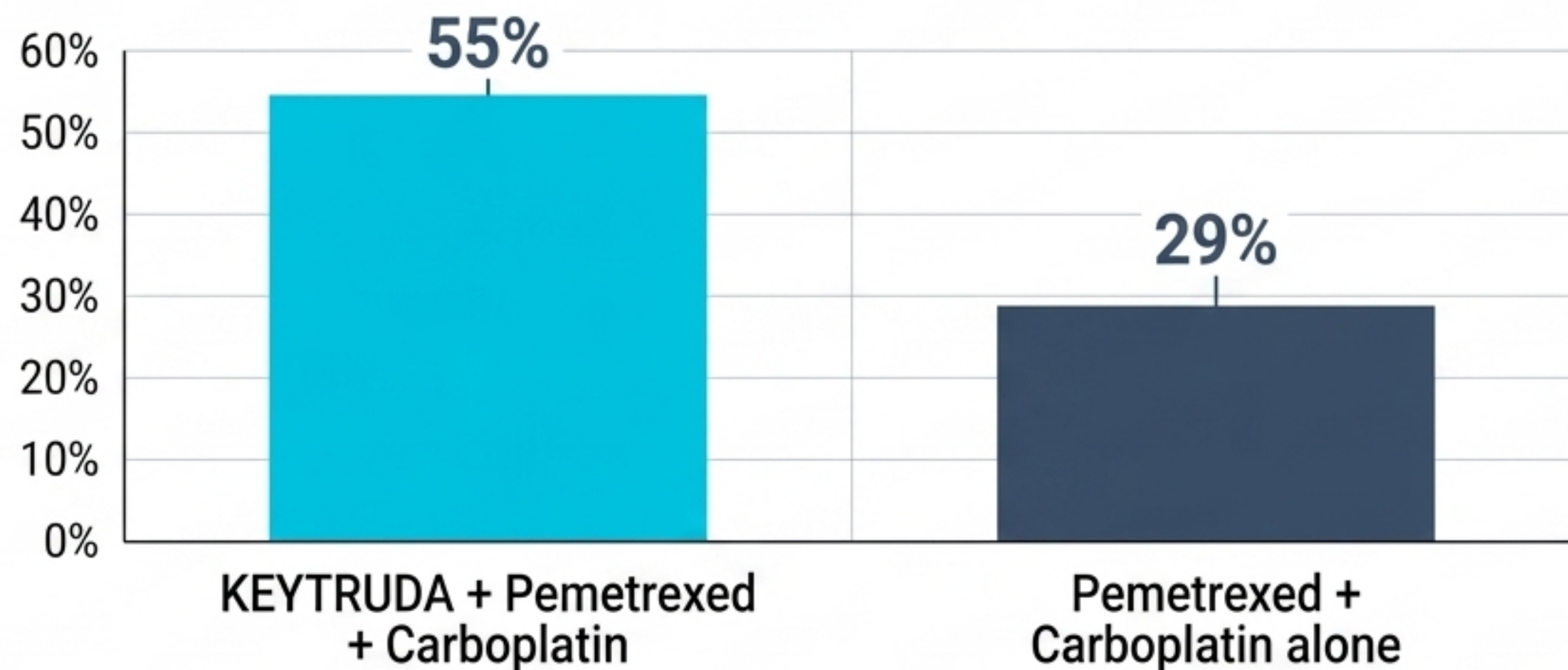
OS HR **0.54/0.50**.
ORR **29-30%**.

Overall TPS $\geq 1\%$:
OS HR **0.71/0.61**.

OS HR **0.71/0.61**.
ORR **18-19%**.

Efficacy Dashboard 3: NSCLC Combination Therapy

KEYNOTE-021 (1st-Line Nonsquamous NSCLC)



Primary Metric (ORR):
55% vs. **29%**

PFS HR: **0.53**
(Median 13.0 months vs. 8.9 months).

Key Context: Efficacy observed regardless of tumor PD-L1 expression.
ORR was 57% in TPS <1% subgroup and 54% in TPS ≥1% subgroup.

Efficacy Dashboard 4: Heavily Pre-Treated Populations

HNSCC (KEYNOTE-012)



Population: Recurrent/Metastatic post-platinum.

ORR: 16% (Complete response 5%).

Durability: Median duration not reached; 23 of 28 responders had responses ≥ 6 months.

cHL (KEYNOTE-087)



Population: Refractory/Relapsed (median 4 prior lines, 61% prior auto-HSCT).

ORR: 69%. Complete Remission: 22%. Partial Remission: 47%.

Durability: Median response duration 11.1 months.

Efficacy Dashboard 5: Urothelial Carcinoma

Patient Eligibility

Cisplatin-Ineligible (KEYNOTE-052)

Setting: 1st line (no cisplatin option).

ORR: 29% (Complete response 7%).

Note: 85% had visceral metastases.

Post-Platinum (KEYNOTE-045)

Setting: 2nd line+ (progressed after platinum).

Comparator: Investigator's choice chemotherapy.

OS HR: 0.73. (Median 10.3 vs 7.4 months).

ORR: 21% vs 11%.

Efficacy Dashboard 6: The Tissue-Agnostic MSI-H Approval



Pooled Efficacy Data (149 patients across 5 trials)

Overall ORR: 39.6%

- **Durability:** 78% of responses lasted ≥ 6 months.

**Colorectal Cancer (CRC)
ORR: 36% (n=90).**

**Non-CRC ORR: 46%
(n=59).**

Patient Selection: Tumors must be tested via PCR (for MSI-H) or IHC (for dMMR). Patients must have progressed following prior treatment with no satisfactory alternatives.

Adverse Reaction Heatmap ($\geq 20\%$ Incidence)

	Melanoma (KN-006)	NSCLC Combo (KN-021)	Urothelial (KN-045)	cHL (KN-087)
Fatigue	28%	71%	38%	26%
Nausea		68%		
Constipation		51%		
Rash	24%	42%		
Diarrhea	26%			
Musculoskeletal pain			32%	
Pyrexia / Cough				24% / 24%

Key Insight: Fatigue is consistently the most universally reported adverse reaction across all monotherapy indications. Combination with chemotherapy drastically elevates GI and fatigue incidence.

Severe Complications & Special Populations



Complications of Allogeneic HSCT

- **Risk:** Fatal immune-mediated complications can occur in patients undergoing allogeneic hematopoietic stem cell transplantation after KEYTRUDA.
- **Data (cHL):** Of 23 patients proceeding to HSCT, 26% developed GVHD (1 fatal), and 9% developed severe hepatic veno-occlusive disease (VOD) (1 fatal).
- **Action:** Follow closely for hyperacute GVHD and steroid-requiring febrile syndrome.



Special Populations

- **Lactation:** Discontinue nursing or discontinue KEYTRUDA (excretion in human milk unknown, but high risk).
- **Pediatric MSI-H CNS Cancers:** Safety and effectiveness not established.

Synthesis: The Evolution of a Foundational Pillar



From Salvage to First-Line Standard

Demonstrated superior OS and PFS against established controls in first-line Melanoma (vs. Ipilimumab) and first-line high PD-L1 NSCLC (vs. Chemotherapy).

The Combination Frontier

KEYNOTE-021 proves that adding KEYTRUDA to platinum doublets effectively doubles the response rate (55% vs 29%) in 1L nonsquamous NSCLC regardless of PD-L1 status.

The Agnostic Paradigm

The MSI-H/dMMR approval validates biomarker-driven, tissue-agnostic prescribing, yielding ~40% response rates in heavily pre-treated, refractory solid tumors.

TAKEAWAY: KEYTRUDA transitions immunotherapy from a late-stage option to a first-line clinical imperative across multiple histologies.