CIMaHer Product Overview

Innokeys

CIMaHer ™
nimotuzumab 50 mg

CIMaHer Product Profile

Brand Name	**CIMaHer**
Composition	Vial contain: Nimotuzumab 50 mg
Dosage Form	Injection
Manufacturer	Centro De Inmunologia Molecular (CIM), La Habana, Cuba
Mechanism of Action	Anti EGFR

Nimotuzumab (Indonesia)

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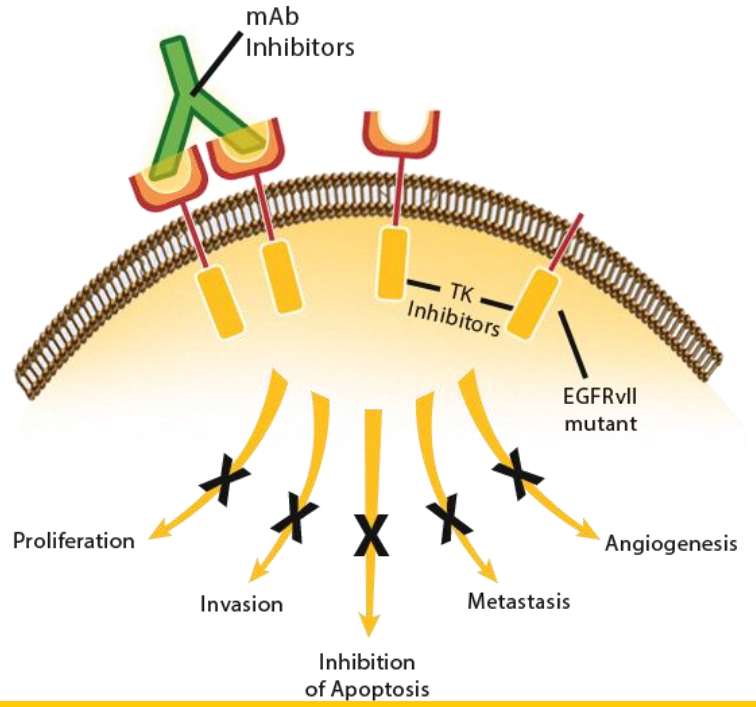
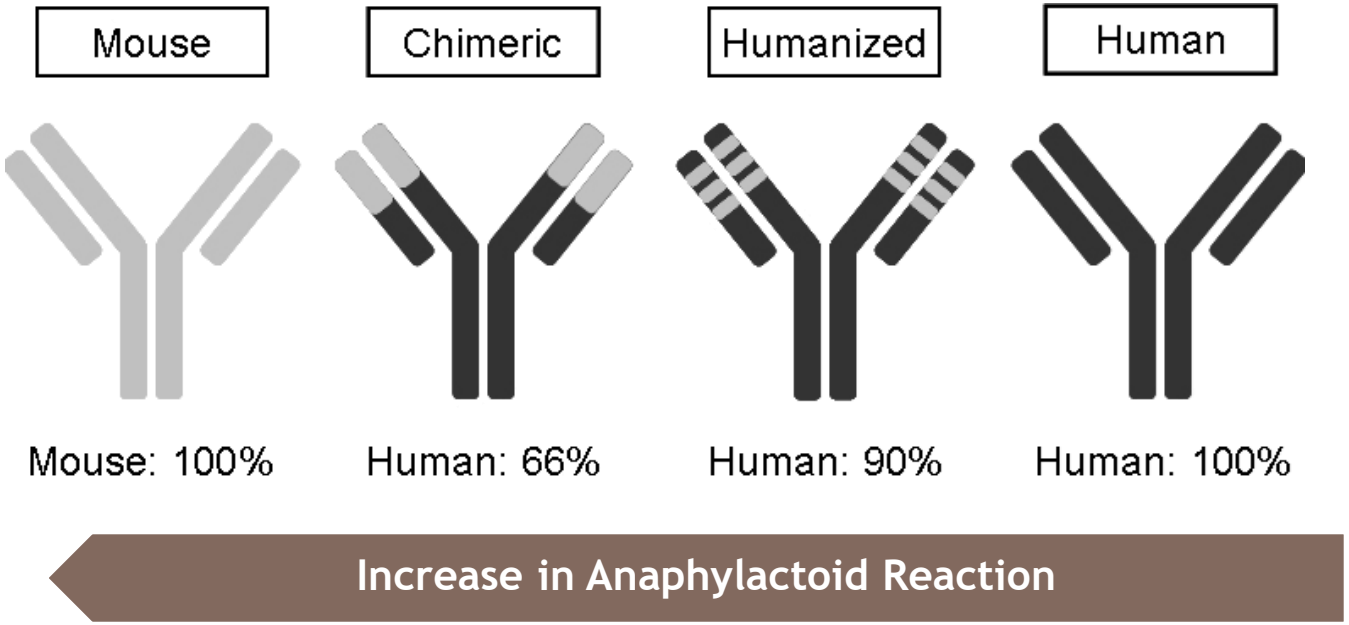
What is Nimotuzumab?

- **Nimotuzumab is humanized IgG1 that target EGFR**
- **Risk of Anaphylactoid Reaction are lower compared to chimeric mAb**





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Nimotuzumab MoA

Block EGFR

Suppress proliferation, angiogenesis, metastastic and improve apoptosis

ADCC

Antibody Dependent Cellular Cytoxicity

Induce cell lysis through NK cell

Vaccinal Effect

Induce T cell memory to fight EGFR

Crombet Ramos et al, Frontiers in Oncology, May 2020, volume 10, article 817

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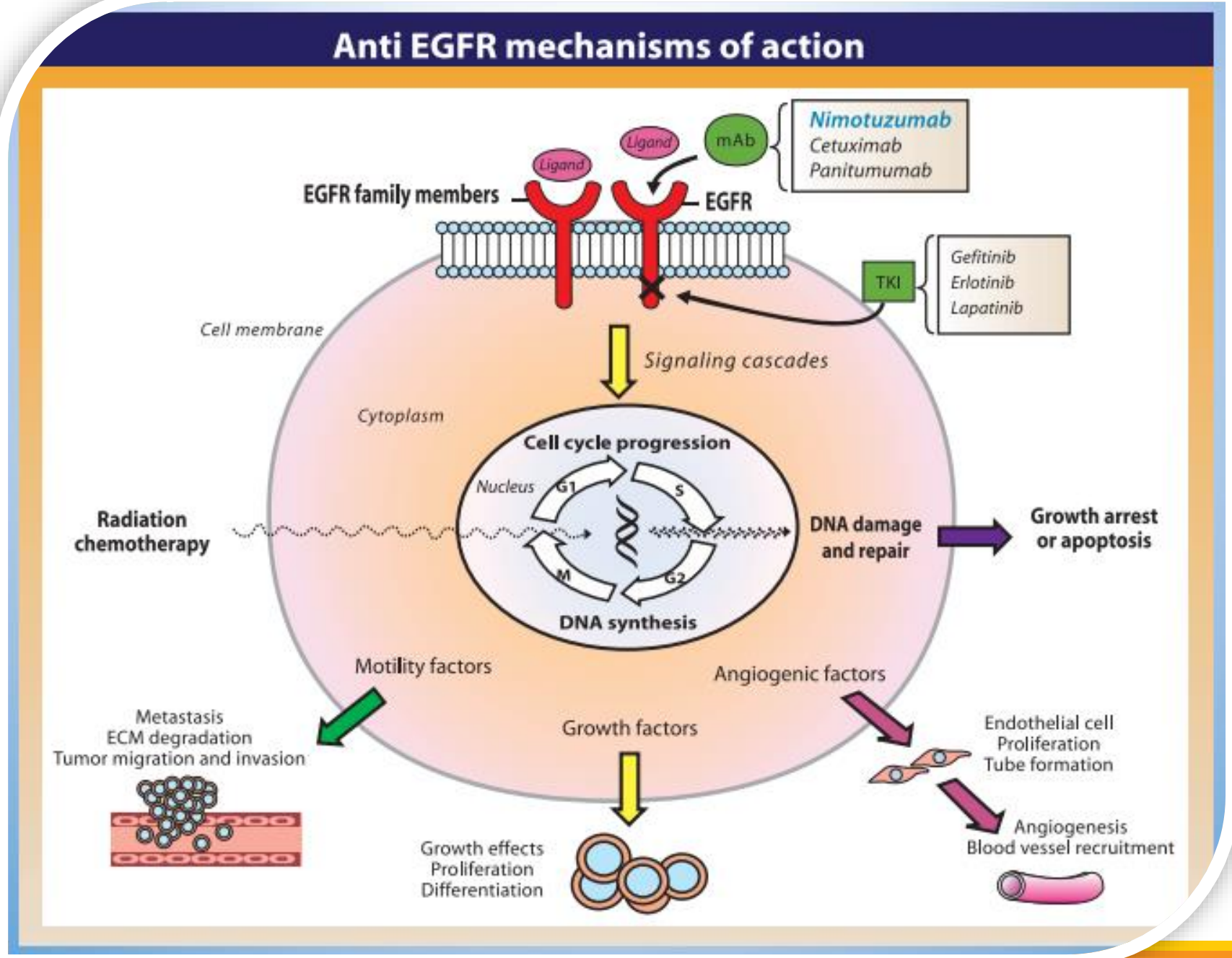

EGFR Blocking

- Nimotuzumab block EGFR therefore EGFR not activated.
- Delay proliferation, angiogenesis, metastasis and improve apoptosis
- Improve radiation effect and chemotherapy

ADCC and vaccine effect

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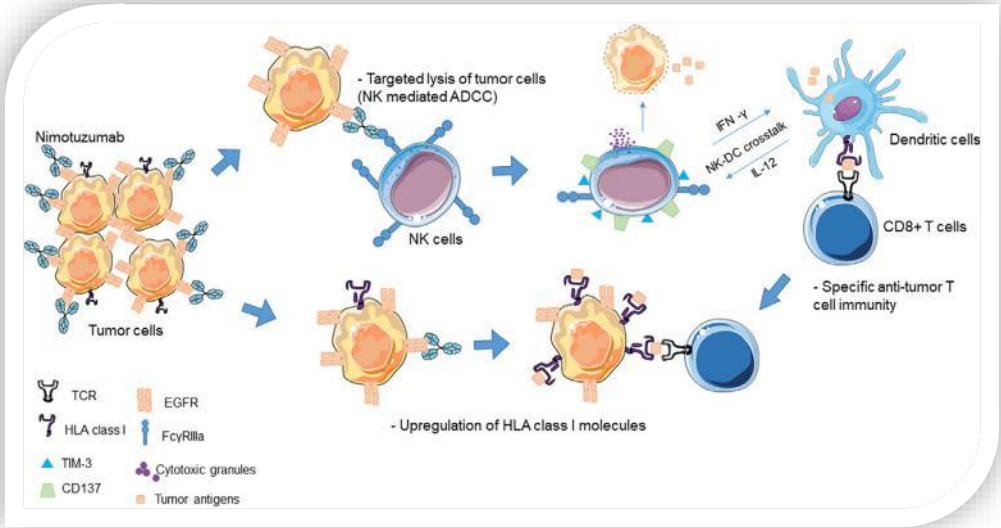
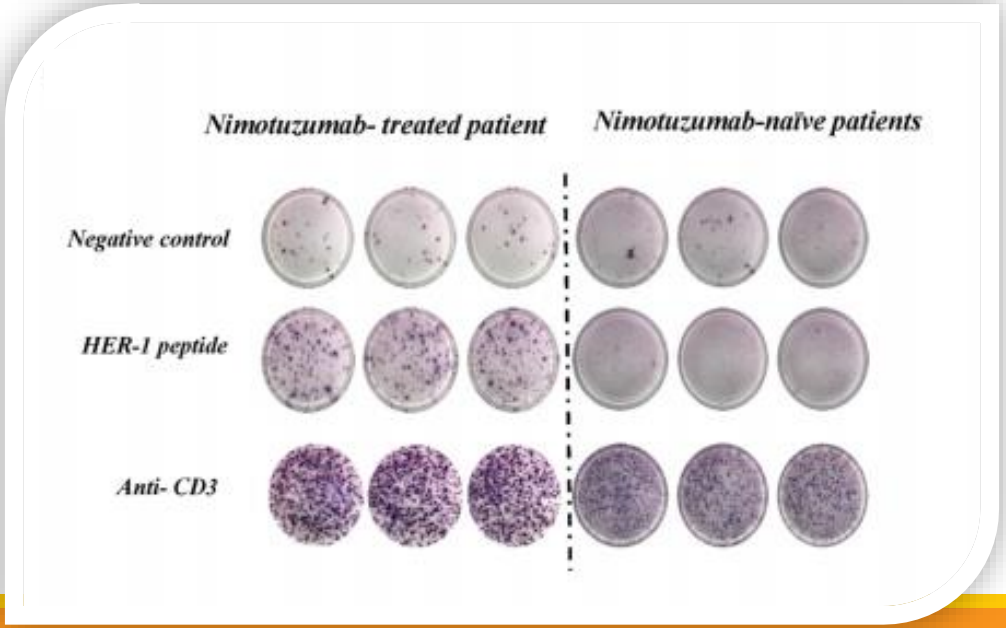


ADCC

Nimotuzumab activate Natural Killer cell (NK) to identify tumor.



Vaccinal Effect

Nimotuzumab promote T cell memory to fight EGFR, responsible for long term clinical effect

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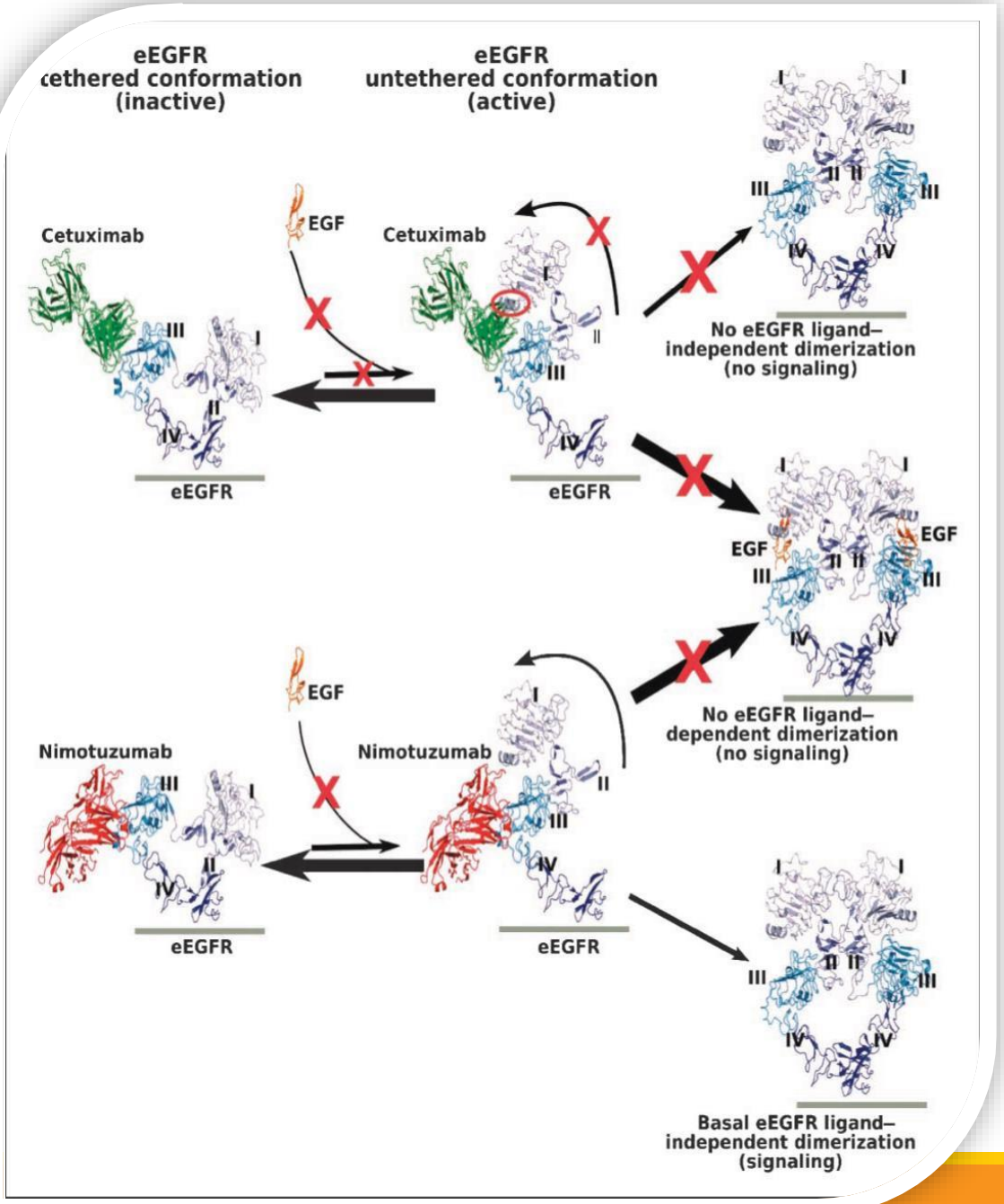

Lower side effect compared to Cetuximab

Binding of Cetuximab to EGFR completely block transduction signal of EGFR, by blocking EGFR both that ligand dependent and not ligand dependent.

Nimotuzumab, on the other hand, blocking EGFR dimerization only on ligand depended, therefore other active EGFR still normally function.

Nimotuzumab – Superior Safety Profile

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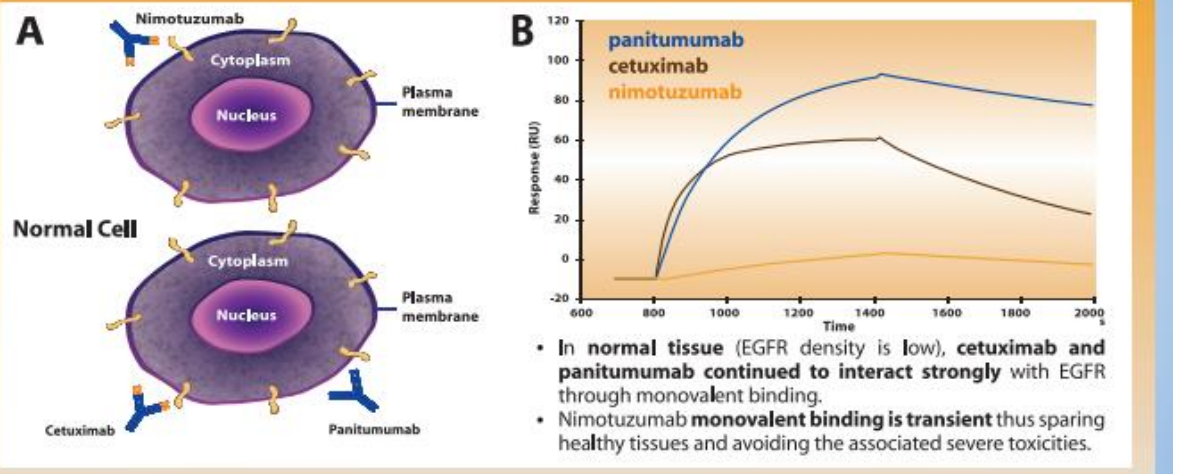
	Erbitux® plus Radiation (n=208)**	Nimotuzumab plus Radiation (n=125)*	Vectibix® plus BSC (n=229)**	BSC Alone (n=234)**
Rash - Grades 3 and 4	17%	Not Observed	14%	0%
Rash* - All grades	87%	**9%**	90%	6%
Pruritus	16%	Not Observed	57%	2%
Hypomagnesemia – Total	50%	Not Observed	39%	2%
Nausea	49%	22%	23%	16%
Diarrhea	19%	9%	21%	1%
Constipation	35%	14%	21%	9%
Vomiting	29%	14%	19%	12%

* Information from four completed trials. Data collection ongoing.

** Information obtained from Erbitux® and Vectibix® product labels

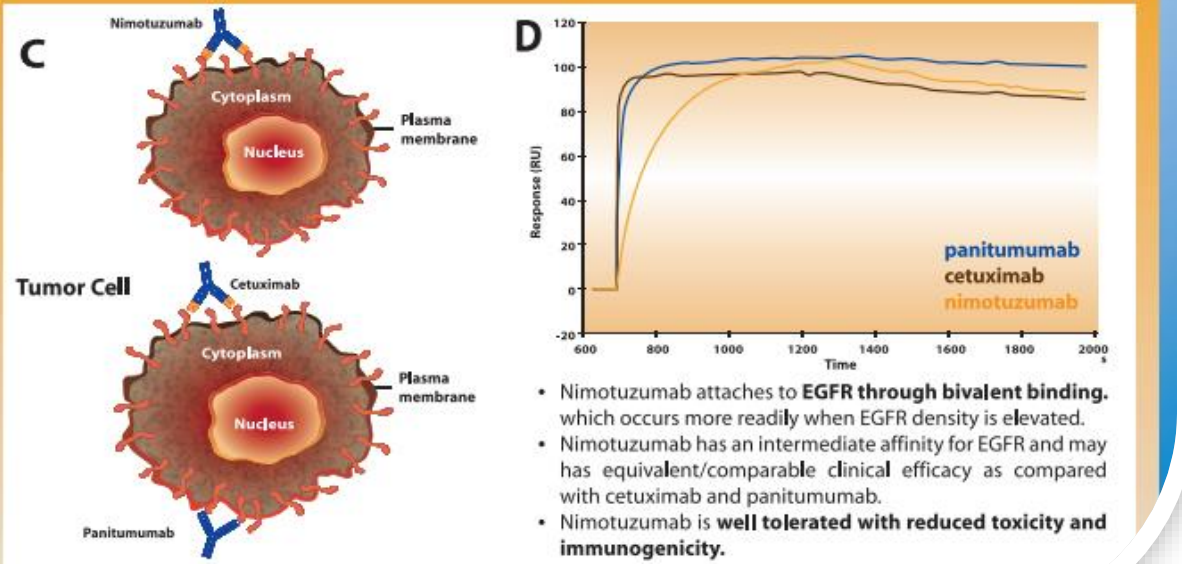
- Affinity-optimised: **activity of Nimotuzumab is concentrated at tumors**
- Nimotuzumab does not cause severe adverse reactions and no grade 3-4 skin rash from the treatment

Selectivity in Normal cells



- In **normal tissue** (EGFR density is low), **cetuximab and panitumumab continued to interact strongly** with EGFR through monovalent binding.
- Nimotuzumab **monovalent binding is transient** thus sparing healthy tissues and avoiding the associated severe toxicities.

Efficacy in tumors



- Nimotuzumab attaches to **EGFR through bivalent binding.** which occurs more readily when EGFR density is elevated.
- Nimotuzumab has an intermediate affinity for EGFR and may has equivalent/comparable clinical efficacy as compared with cetuximab and panitumumab.
- Nimotuzumab is **well tolerated with reduced toxicity and immunogenicity.**

Lower side effect compared to other Anti-EGFR

Nimotuzumab have optimal affinity binding, therefore can selectively work based on EGFR density.

Nimotuzumab give effect on tumor cell that have high density of EGFR, but didn't give effect on normal cell that have low EGFR density.

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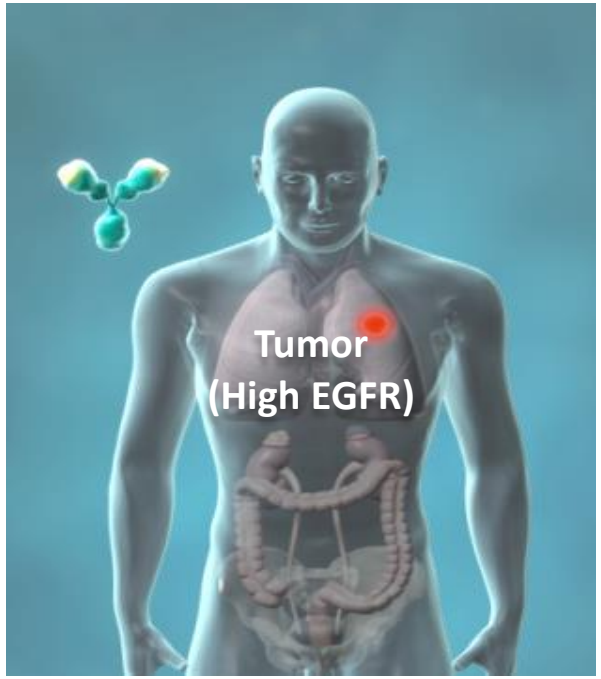
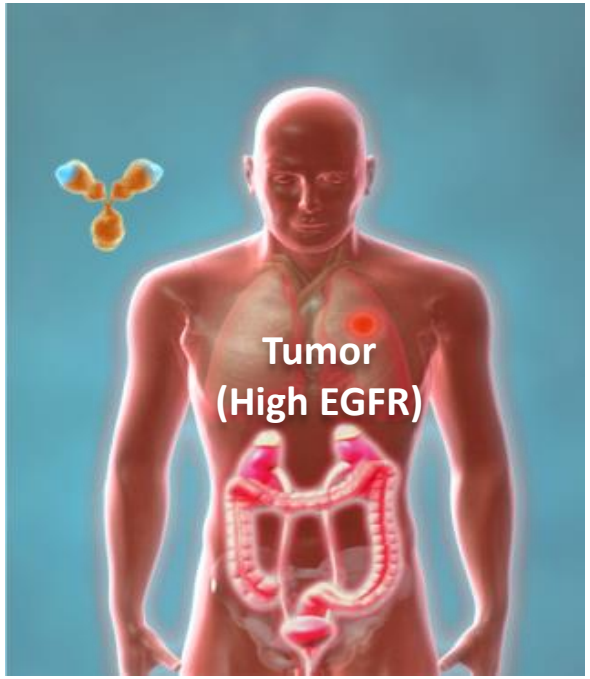
Nimotuzumab – Mechanistically Differentiated

Activity of Nimotuzumab is concentrated at tumor



Nimotuzumab
Affinity-Optimized™ Ab

Activity of high affinity anti-EGFR Abs is dispersed across all tissues, causing toxicity



High Affinity
anti-EGFR Abs

EGFR as Target

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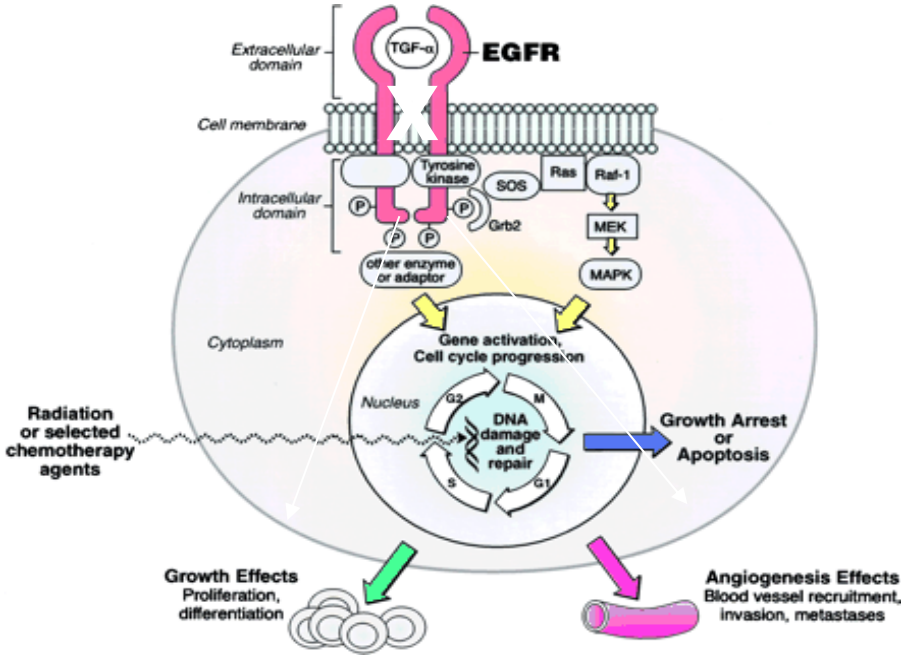

Tumor type	Percentage of tumors overexpressing EGFR
Colon	25–77%
Head and neck	80–100%
Pancreatic	30–50%
Nonsmall cell lung carcinoma	40–80%
Breast	14–91%
Renal carcinoma	50–90%
Ovarian	35–70%
Glioma	40–63%
Bladder	31–48%

- ***Increases invasive capacity***
- ***Increasing proliferation***
- ***Blocks apoptosis***
- ***Increases motility and adhesion***
- ***Promotes angiogenesis***

Cunningham et al, NEJM 2004. Grandis et al, *Cancer* 1996. Salomon et al, *Crit Rev Oncol Hematol* 1995. Walker & Dearing, *Breast Cancer Res Treat* 1999.

Combining Radiotherapy and Systemic Therapy