Achievements in formulation of stable immunoconjugate of the HER2-targeting trastuzumab – potential for rapid labelling with Gallium-68

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Introduction:

Trastuzumab → humanized IgG1 monoclonal antibody.
Targeting HER2 positive breast cancer.
Good clinical results → further conjugation.
First success → conjugation with cytotoxic drug - *emtansine*.

Successful conjugation is achieved with:

p-SCN-Bn-DOTA((1-(4-izothiocyanatobenzyl)-1,4,7,10-tetra-azacyclododecane-1,4,7,10-tetraacetic acid),
p-SCN-Bn-DTPA((1-(4-izothiocyanatobenzyl)diethylenetri-aminepentaacetic acid),
TCMC(1,4,7,10-tetra-(2-carbamoyl methyl)-cyclododecane),
HYNIC(succinimidyl-6-hydrazino-nicotinamide) and
1B4M-DTPA(2-(4-izothiocyanatobenzyl)-6-methyl-diethylene-triaminepentaacetic acid).

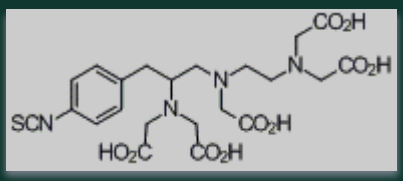

Fig. 1 p-SCN-Bn-DTPA

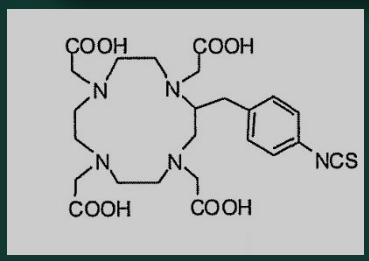

Fig. 2 p-SCN-Bn-DOTA

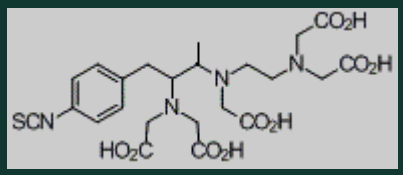

Fig. 3 1B4M-DTPA

Radioimmunodiagnostic agents - **γ emitters** (^{111}In, ^{99m}Tc/^{188}Re, ^{64}Ga, ^{67}Ga and ^{68}Ga).
Radioimmunotherapeutic agents - **α** and **β emitters** (^{90}Y, ^{86}Y, ^{177}Lu, ^{227}Th, ^{225}Ac)
^{90}Y-DTPA-trastuzumab, ^{86}Y-DTPA-trastuzumab, ^{177}Lu-DOTA-trastuzumab, ^{227}Th-DOTA-p-benzil-trastuzumab, ^{225}Ac-trastuzumab

Results:

Obtained and published results related to the method for production of “ready to use” freeze dried kit formulation of Rituximab imunnoconjugates (p-SCN-Bn-DOTA, p-SCN-Bn-DTPA and 1B4M-DTPA) for labeling with Lu-177 and Y-90

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Good reason to introduce the same approach for labeling HER2-targeting trastuzumab using $^{68}Ga^{3+}$ for PET imaging.

Fig. 4 Ga-68 Generator

Discussion:

Work progress and achievements listed under our project are:
1. Standardize previously established method used for freeze dried kit formulation of Rituximab imunnoconjugates for HER2-targeting trastuzumab imunnoconjugates.
2. Conjugation of bifunctional chelators for HER2-targeting trastuzumab, and radiolabeling with Ga-68.
3. In vitro characterization and in vivo biodistribution of ^{68}Ga-labeled conjugates.

Conclusion:

Introducing the established method for freeze dried kit formulation of conjugated rituximab (for labeling with Lu-177, Y-90), for labeling the HER2-targeting trastuzumab.
The simplicity and efficiency of labelling with ^{68}Ga tracer will greatly increase ^{68}Ga PET access to hospitals, expanding the use of the ^{68}Ga generator.
In the same time give opportunity to work on the same or similar kit formulation using with Lu-177 for therapy.

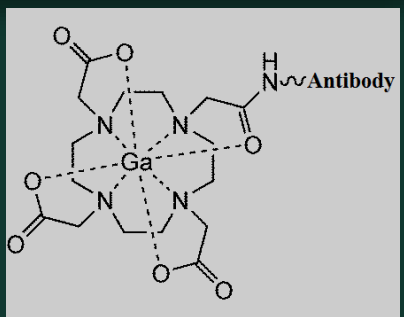

Fig. 5 Ga-68 labeled Trastuzumab-DOTA