

ASSESSMENT OF HER2 HETEROGENEITY IN MBC WITH A NOVEL PET TRACER

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ABOUT ABSCINT



- ABSCINT is a clinical stage company specializing in molecular imaging technologies
- The company develops *in vivo* diagnostics using single-domain antibodies, enhancing diagnostic precision
- Our lead program is around the visualization of HER2

For more information, visit Abscint's website at https://abscint.com/

TECHNOLOGY PLATFORM: MOLECULAR IMAGING BASED ON SINGLE-DOMAIN ANTIBODIES



TECHNOLOGY PLATFORM: MOLECULAR IMAGING BASED ON SINGLE-DOMAIN ANTIBODIES

Single-domain antibodies (sdAb)

- Antibody fragment consisting of a single monomeric variable antibody domain
- Also called Nanobody[™]



TECHNOLOGY PLATFORM: MOLECULAR IMAGING BASED ON SINGLE-DOMAIN ANTIBODIES

		Labeled therapeutic antibodies	ABSCINT sdAb
	Ease of Use Injection and scan on same day	NO (4 days)	YES
Ũ	In competition with binding pockets of therapeutic antibodies	YES	ΝΟ
	Irradiation burden for patient	HIGHER	LOW
0	Production process optimized for high yield	YES	YES
€	Cost-of-goods	HIGHER	LOWER
>>>>	Stage of development	Generic product	Clinical studies ongoing

ANTI-HER2 PET TRACER [68GA-ABS011]

ANTI-HER2 PET TRACER

The importance of Human epidermal growth factor receptor 2 (HER2)

- HER2 is a growth promoting protein expressed on different types of cancer cells, including breast cancer, GI cancer, lung cancer,
- Cancer cells with higher-than-normal levels of HER2 are called HER2-positive
- These cancers tend to grow and spread faster than other breast cancers, but are much more likely to respond to treatment with drugs that target the HER2 protein
- Treatment decisions are based on HER2 profile of patients

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SOME CASE STUDIES WITH ANTI-HER2 PET TRACER



Image of a metastatic breast cancer patient with only brain metastases (7 lesions in total)

Breast cancer patient with HER2 low disease (IHC 2+ / ISH NA). The HER2 PET scan shows intense uptake in bone metastases. HER2-PET shows more lesions than FDG-PET.





Image of a gastric cancer patient with HER2 expressing metastases

Breast cancer patient originally diagnosed as HER2-negative (IHC 0). The HER2-PET scan however indicates HER2-positive bone metastases which were confirmed to be IHC 2+ after biopsy. The HER2-PET scan shows uptake in metastases in bone, lung and liver.

FDG-PET

HER2-PET

FDG-PET

HER2-PET

HER2-PET

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ANTI-HER2 PET TRACER: CLINICAL NEED

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Current approach in determining HER2 status of cancer cells

Perform biopsy on one lesion and determine HER2 expression by immune-histochemistry (IHC)



ANTI-HER2 PET TRACER: CLINICAL NEED

Limitation of current biopsy-based approach:

- HER2 expression is not uniform throughout the body (inter-tumor heterogeneity)
- HER2 expression can change over time (temporal heterogeneity)
- Not all lesions are accessible for (reliable) biopsy + IHC

Only whole-body *in-vivo* imaging is able to provide a comprehensive view of all lesions or anomalies present in a patient



INTER-LESION HETEROGENEITY WITHIN ONE PATIENT CANNOT LONGER BE DENIED



CURRENT PROBLEM INCORRECT HER2 STATUS CLASSIFICATION TRIGGERED BY HER2 HETEROGENEITY

Current HER2 categorization (what SOC assumes reality is):

- Relies on 1 tumor lesion biopsy
- Assumes a homogeneous status



In vivo imaging shows that reality is more complex



Only whole-body imaging shows reality

Heterogeneity is present in all three HER2 categories and is most outspoken in the HER2 low patients

CURRENT PROBLEM HER2 HETEROGENEITY DRIVES INCORRECT DIAGNOSIS OF HER2 STATUS

CASE A: False negative HER2 diagnosis?

- Patient diagnosed as HER2-negative (null) based on a single biopsy
- Patient will NOT benefit from HER2-targeted treatment, despite presenting potential HER2 lesions elsewhere in the body
- Due to the absence of proper treatment, HER2 cancer lesions may progress

→ Undertreatment



CASE B: False positive HER2 diagnosis?

- Patient diagnosed as HER2-low based on a single biopsy
- Patient will receive HER2targeted treatment, despite presenting mostly HER2-negative (null) lesions
- Due to the absence of proper treatment, cancer lesions may progress
- Patient may also suffer from adverse events due to the toxicity of the HER2-targeted treatment







HER2 heterogeneity

- HER2 status in breast cancer patients is not uniform throughout the body
- Lesion selection bias drives erroneous HER2 diagnosis
- Only molecular imaging might provide correct picture of whole body HER2 status



HER2 nullHER2 low or positive



The 3 patient cases can have the same IHC/ISH based score but will likely react differently on HER2 targeted therapy due to different % of HER2 positive lesions

ANTI-HER2 PET TRACER: PATIENT JOURNEY

Example 1: Reclassification via image guided biopsy



Metastatic breast cancer patient initially diagnosed with HER2 null (IHC 0) but rapidly progressing (heterogeneity)

Conclusion

- Patient has evolved from HER2 null to HER2 low (IHC 2+)
- ABSCINT-HER2 sensitive to show HER2 low lesions
- Neck lesion shows tumor heterogeneity

Patient 63 years old woman

2012 <u>Status</u>: Invasive lobular carcinoma (ILC) breast cancer <u>Biopsy</u>: neck lesion HER2 null IHC 0

2017-2019 Status: Progressing disease

2019 <u>In vivo diagnostic</u>: FDG-PET vs. **ABSCINT-HER2** PET/CT **ABSCINT-HER2**: moderate to high, heterogeneous tracer uptake (bone, adenopathy, muscle invasion)

Additional bone metastases revealed with **ABSCINT-HER2** vs. FDG

<u>Biopsy</u>: neck lesion HER2 low IHC 2+



ANTI-HER2 PET TRACER: PATIENT JOURNEY

Example 2: Patient follow-up



Treatment response follow-up Neoadjuvant therapy in HER2+ breast cancer with lymph node involvement

Objective

- Monitoring of neoadjuvant therapy in HER2+ breast cancer patients for decision around lymphadenectomy
- Example: grade II invasive ductal mammary carcinoma of the left breast, neoadjuvant therapy combined with chemotherapy

Current problem

- Partial and incomplete diagnosis with FDG-PET
- Unsuitable for monitoring of treatment efficacy or disease progression

Solution

- ABSCINT technology, PET scan
- High specificity, resolution and reproducibility
- Suitable for monitoring

Outcome

- Provide a good rationale for decision
 - Important to avoid recurrence of disease
 - Avoid unnecessary lymphadenectomy, which can lead to lymphedema (swollen and tight-feeling arm, pain, numbness), in 20-30% of cases [1]

Pre-treatment

ABSCINT-HER2

ABSCINT-HER2

FDG



[1] Canadian Cancer Society – <u>Website</u> Lymphedema After Breast Cancer: Incidence, Risk Factors, and Effect on Upper Body Function – <u>Article</u>

ANTI-HER2 PET TRACER: ONGOING PHASE IIB CLINICAL STUDY

STUDY ENDPOINTS:



2. **Treatment change** before and after evaluation of ABS011 PET/CT

3. **Prognostic performance:** Evaluate whether HER2 positive lesions react well to HER2 targeted therapy i.e. treatment success based on FDG PET CT (early metabolic response) and CT (early tumor shrinkage)



DIAGNOSTIC PHASE

SOCa TREATMENT FU PHASE



CLINICAL ABSCINT-HER2 MATERIAL IS NOW AVAILABLE

Are you interested in learning more about our [⁶⁸Ga] ABSCINT-HER2 product? Or interested in using it?



ABSCINT can provide material for:

- Research use
- Compassionate use
- Investigator-driven clinical studies

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THANK YOU FOR YOUR ATTENTION