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Reporting on invasive lobular breast cancer in clinical drug trials and trials investigating gene expression profiles and molecular screening programs: a systematic review

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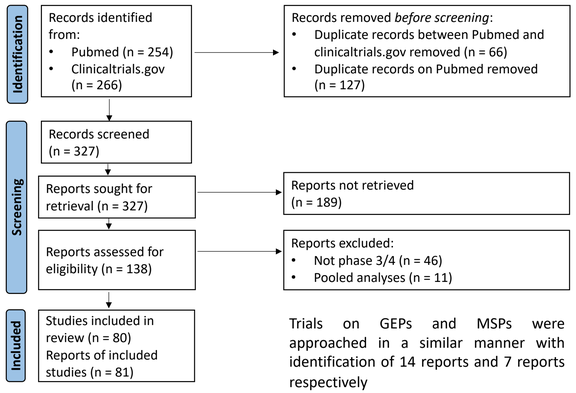
BACKGROUND and AIMS

- ILC represents 15% of all breast cancers[1]
- ILC needs to be seen as a separate entity as it differs from NST on a clinical, pathological and biological level[1]
- Differences in treatment response between ILC and NST have been described for chemotherapy[2]
- There is a lack of knowledge for treatment efficacy of novel breast cancer treatment in patients with ILC[1]
- Patients with ILC might be underrepresented in clinical trials, especially in case of stage IV disease[3]
- The unique growth pattern and metastatic pattern of ILC more often leads to non-measurable disease while RECIST criteria are commonly used as inclusion criteria for drug trials[1,3,4]

Here we aimed to map out the lack of documentation and representation of patients with ILC in clinical drug trials and trials investigating GEPs

METHODS

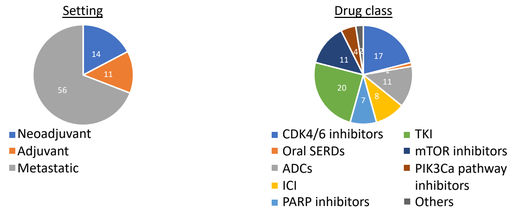
- Identification of phase 3/4 clinical trials for novel breast cancer treatments by use of keywords linked to treatment strategies, GEPs, molecular screening programs (MSP) and 'breast cancer'
- Inclusion of trials if a full manuscript was available on the 15th of January 2023
- Review of inclusion and exclusion criteria to see if patients with ILC or non-measurable disease were excluded
- Assessment of documentation on ILC: percentage included, central pathology and subgroup analyses



Trials on GEPs and MSPs were approached in a similar manner with identification of 14 reports and 7 reports respectively

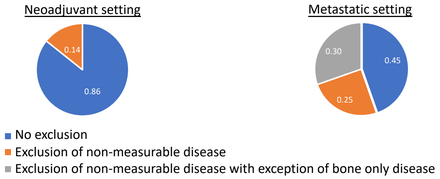
RESULTS

Features of clinical trials



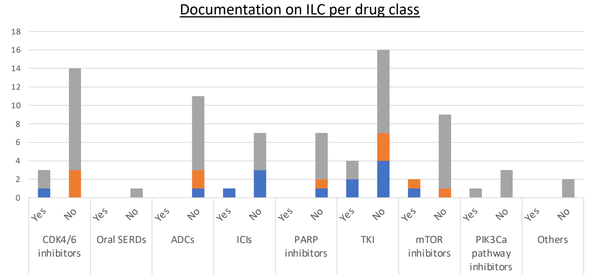
Inclusion and exclusion criteria in clinical trials

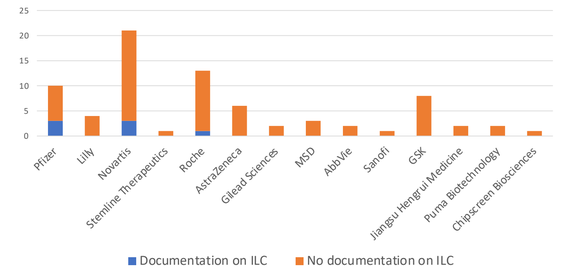
1/81 trials included exclusively patients with NST
Inclusion/exclusion based on measurable disease:



ILC documentation in clinical trials

In total 13,6% of the trials reported the percentage of patients with ILC included: 35,7% in neoadjuvant, 9,1% in adjuvant and 8,9% in metastatic setting



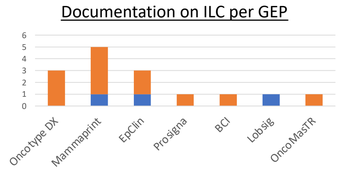


ILC representation in clinical trials

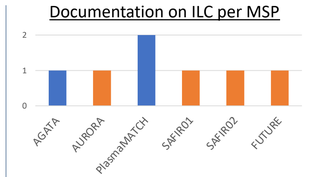
Setting	Trial	Drug	Patient population	% ILC included	Subanalysis	Central pathology
Neoadjuvant	SAFIA	Palbociclib (CDK4/6i)	HR+ HER2-	12	No	No
	IMpassion031	Atezolizumab (ICI)	TNBC	2	No	No
	GeparQuinto - Lapatinib	Lapatinib (TKI)	HR- HER2+ or HR+ HER2+ if cN+	2,76	Yes	No
	EPHOS B	Lapatinib (TKI)	HER2+	4	No	No
	GeparQuinto - Everolimus	Everolimus (mTORi)	HR- HER2+ or HR+ HER2+ if cN+	10,8	Yes	No
Adjuvant	MAINtenance Afinitor	Everolimus (mTORi)	HR+ HER2-	16,3	No	No
Metastatic	PALOMA 2*	Palbociclib (CDK4/6i)	HR+ HER2-	14,7	No	No
	PALOMA 4*	Palbociclib (CDK4/6i)	HR+ HER2-	3,8	No	No
	NCT00281658**	Lapatinib (TKI)	HER2+	4,73	No	No
	DETECT III	Lapatinib (TKI)	HER2- with HER2+ CTCs	9,8	No	No
	BELLE-2	Buparlisib (PI3Ki)	HR+ HER2-	13	No	No

*Exlusion non-measurable disease with exclusion of bone only disease; **Exclusion of non-measurable disease

ILC documentation and representation in trials on GEPs and MSPs



- No subgroup analyses were performed in the trials (with documentation on ILC) evaluating Mammaprint and EpClin.
- Lobsig was specifically designed for ILC.



- AGATA and PlasmaMATCH included 7,3 and 9,3% patients with ILC respectively.

CONCLUSIONS

ILC is greatly overlooked in the majority of clinical trial with
- poor documentation
- poor representation
- lack of specific sub-analyses
- lack of central pathology

Eligibility criteria and definitions of treatment response in clinical trials do not reflect the unique biology and clinical course of ILC.

Only few retrospective trials asses the use of novel breast cancer therapies for patients with ILC

Most of the GEPs have been developed without considering the specific aetiology and histology of ILC. Secondary trials confirm the prognostic value of some of these GEPs for patients with ILC. For the MSPs, 2/3 reported the prevalence of ILC in the patients included.

ILC deserves much more attention from both clinical investigators and pharmaceutical industries.

ABBREVIATIONS

- ADC: antibody drug conjugate
- GEP: gene expression profile
- ICI: immune checkpoint inhibitors
- ILC: invasive lobular carcinoma
- NST: breast cancer of non-special type
- RECIST: response evaluation criteria in solid tumours
- SERD: selective oestrogen receptor degrader
- TKI: tyrosine kinase inhibitors

REFERENCES

[1]Van Baelen K. *et al.*; Ann Oncol 2022; 33, 769-785
[2]Timbres J. *et al.*; Cancers 2021; 13, 3036
[3]Abel M.K. *et al.*; NPJ Breast Cancer 2021, 7, 139
[4]Eisenhauer E.A. *et al.*; Eur. J. Cancer 2009; 45, 228-247

ACKNOWLEDGEMENTS

The authors like to thank all contributors from the Lobular Breast Cancer Alliance (LBCA) and the European Lobular Breast Cancer Consortium (ELBCC) and Lobsterpot. This article/publication is based upon work from COST Action LOBSTERPOT CA19138, supported by COST (European Cooperation in Science and Technology, http://www.cost.eu/).

JVC is funded by the KU Leuven Fund Nadine de Beauffort.

KVB is funded by the KU Leuven Fund Nadine de Beauffort and a Conquer Cancer – Lobular Breast Cancer Alliance Young Investigator Award for Invasive Lobular Carcinoma Research, supported by Lobular Breast Cancer Alliance. Any opinions, findings, and conclusions expressed in this material are those of the author(s) and do not necessarily reflect those of the American Society of Clinical Oncology® or Conquer Cancer®, or Lobular Breast Cancer Alliance.

♥ We like to dedicate this work to Leigh Pate and Deborah Mueller, 2 amazing women who have meant so much for the ILC community and who will be greatly missed ♥