

Evaluating the effect of Metformine on Breast Cancer

From the clinic to the bench ...

A single center review

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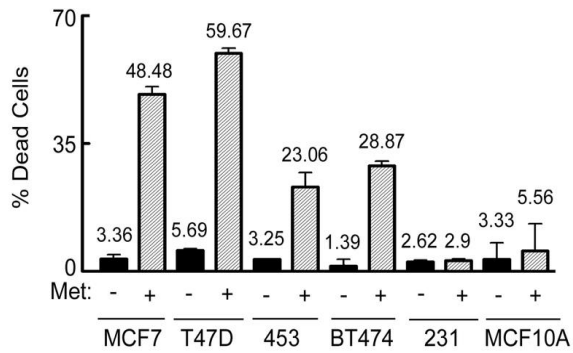
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No disclosures

BACKGROUND

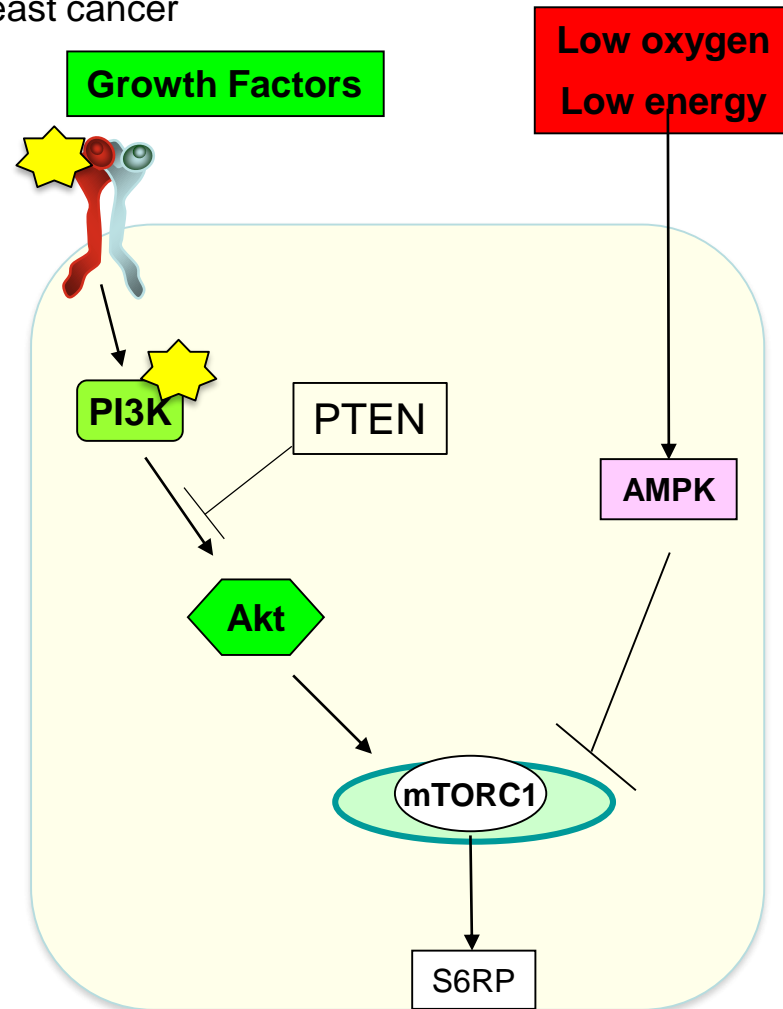
- Breast cancer is the most common cancer in woman
- The PI3K-AKT-mTOR plays a key role in cell survival, proliferation and angiogenesis
- The PI3K-AKT-mTOR cascade is frequently activated in breast cancer
- Metformine decreases mTOR activity via AMPK axis



Molecular Cancer Research 2011

In Clinic, effect of metformine on

- Breast cancer evolution ?
- Anticancer chemotherapy ?



Hypothesis 1

Retrospective analysis in 'Hopital de Jolimont'

Patients with diagnosis of breast cancer between January 2017 and June 2019

All Diagnosis of invasive BCa

Stratification based on

- Metformine user (start at least 1ybefore Bca)
- Metformine non-user

Characteristics of tumors:

Luminal, Triple -, HER2

Tumor size

Metformine associated with less
advanced/ aggressive Bca ?

Néoadjuvant Chemo for BCa

Stratification based on

- Metformine user
- Merformine non-user

Exclusion of HER2+ and Triple -

Metformine increases efficacy
of chemotherapy ?

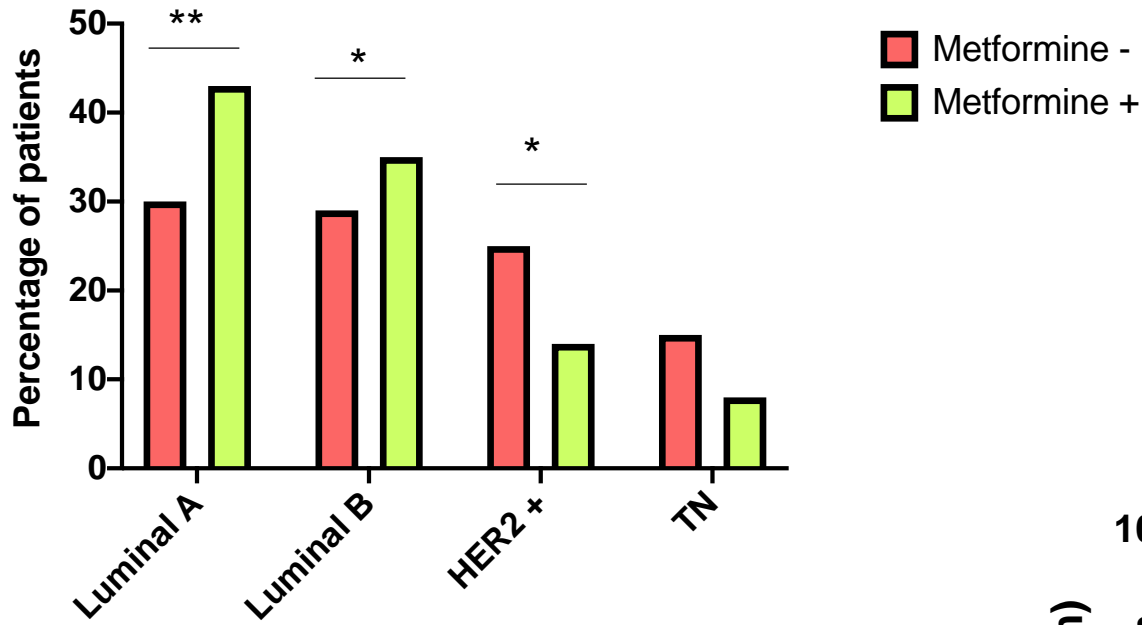
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Metformine associated with less aggressive/advanced breast Cancers ?

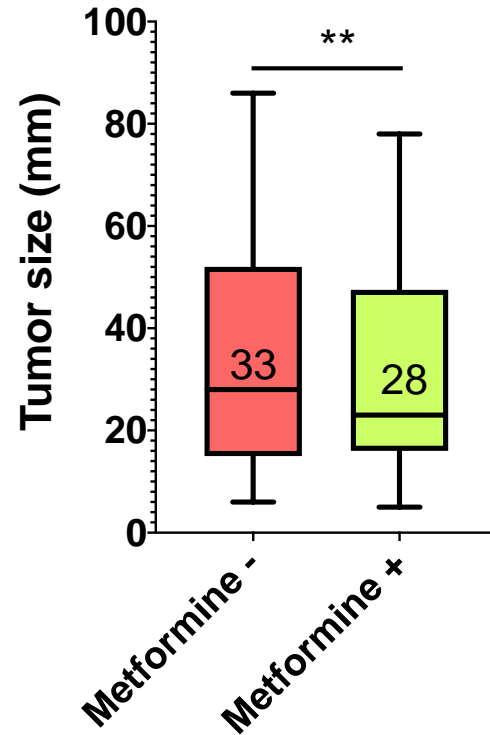
254 patients with invasive breast cancer

Characteristics	Metformine USERS n=49	Metformine Non Users n= 205
- Median age (range)	70 (40-89)	65 (26-87)
- Ductal	40 (82)	175 (85)
- Lobular	9 (18)	30 (14)
- Luminal A	21 (43)	63 (30)
- Luminal B	17 (35)	60 (29)
- HER2	7 (14)	51 (25)
- Triple negative	4 (8)	31 (15)
- Well Differentiated	13 (27)	60 (29)
- Moderately differentiated	25 (51)	85 (41)
- Poorly differentiated	10 (20)	60 (29)
pT1 –T2	36 (73)	132 (65)
pT3 T4	13 (26)	73 (35)
pN-	34 (69)	117 (57)
pN+	15 (31)	88 (43)

BCa type based on Metformine Use



Tumor size based on Metformine use



Hypothesis 2

Retrospective analysis in 'Hopital de Jolimont'

Patients with diagnosis of breast cancer between January 2017 and June 2019

All Diagnosis of invasive BCa

Stratification based on

- Metformine user
- Merformine non-user

Characteristics of tumors:
Luminal, Triple -, HER2

Exclusion of intraductal

Metformine associated with less
advanced/ aggressive Bca ?

Néoadjuvant Chemo for BCa

4 EC → TAXOL

Stratification based on

- Metformine user
- Merformine non-user

Evaluation of tumor decrease

Exclusion of HER2+ and Triple -

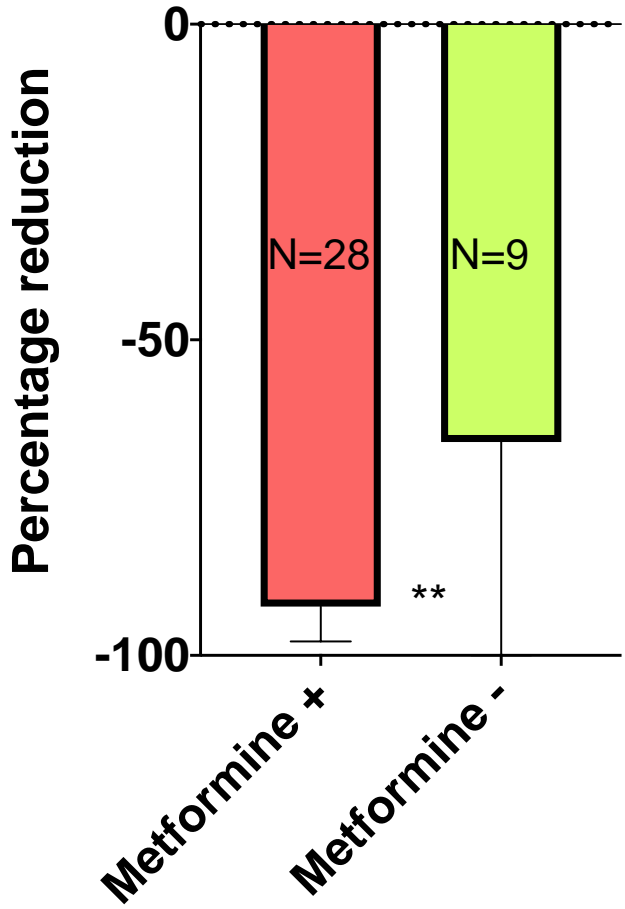
Metformine increases efficacy
of chemotherapy ?

2

Metformine increases the efficacy of Neoadjuvant Chemo in Bca ?

Characteristics	Metformine USERS n=9	Metformine Non Users n=28
Luminal A Lumina B	1 (11) 8 (89)	2 (7) 26 (93)
N- N+	3 (33) 6 (66)	8 (29) 20 (71)
T1-T2 T3-T4	2 (22) 7 (78)	3 (11) 28 (89)
Grade 1 Grade 2 Grade 3	0 (0) 5 (55) 4 (45)	0 (0) 13 (46) 15 (54)
HER2 and TN were excluded	0 (0)	0 (0)
Complete cycle received	8 (89)	27 (96)

Percentage change in tumor size on neoadjuvant chemotherapy



pCR in Metformine - = 7%

pCR in Metformine + = 33%

P=.04

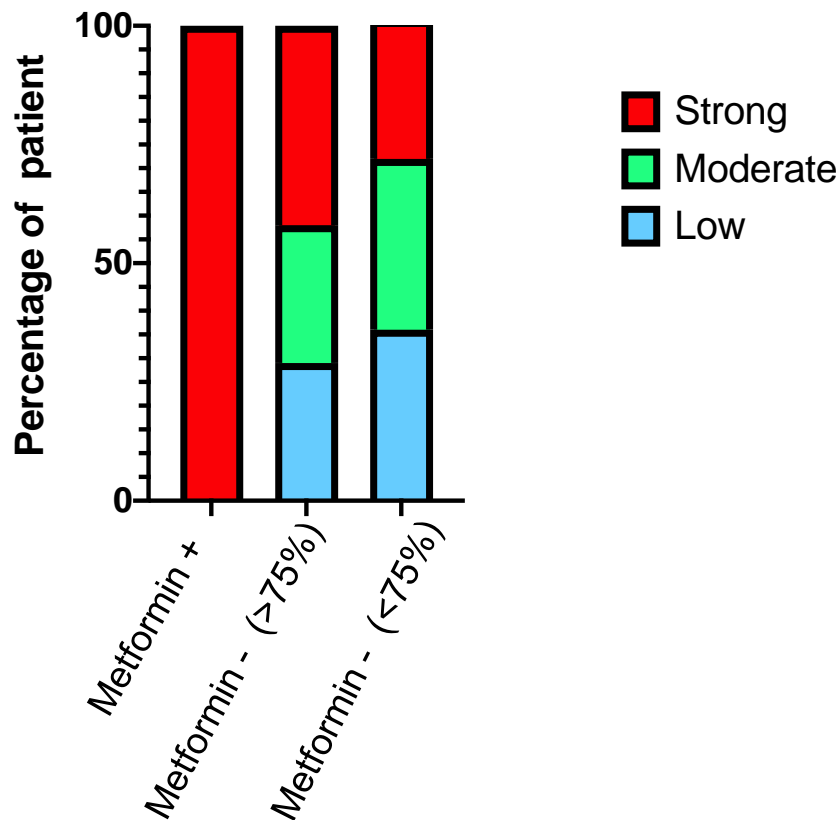
Focus on exploratory analysis of PRE and POST chemotherapy samples

Good responders > 75% of reduction in tumor size with chemo

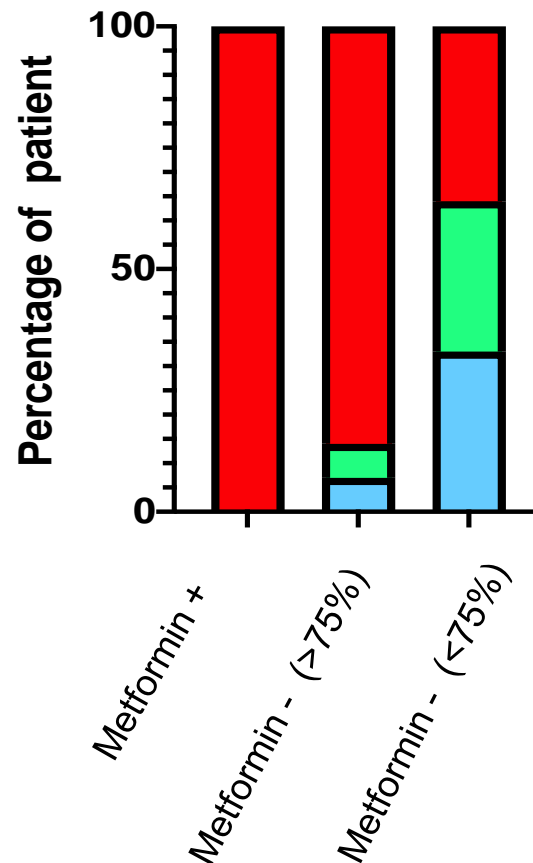
Moderate responders ≤ 75% of reduction in tumor size with chemo

	Metformine + N=8 (%)	Metformine – N=28 (%)
Good responders	8 (100)	14 (50)
Moderate responders	0	14 (50)

**H-Score of p-AMPK
in pre-chemotherapy sample**



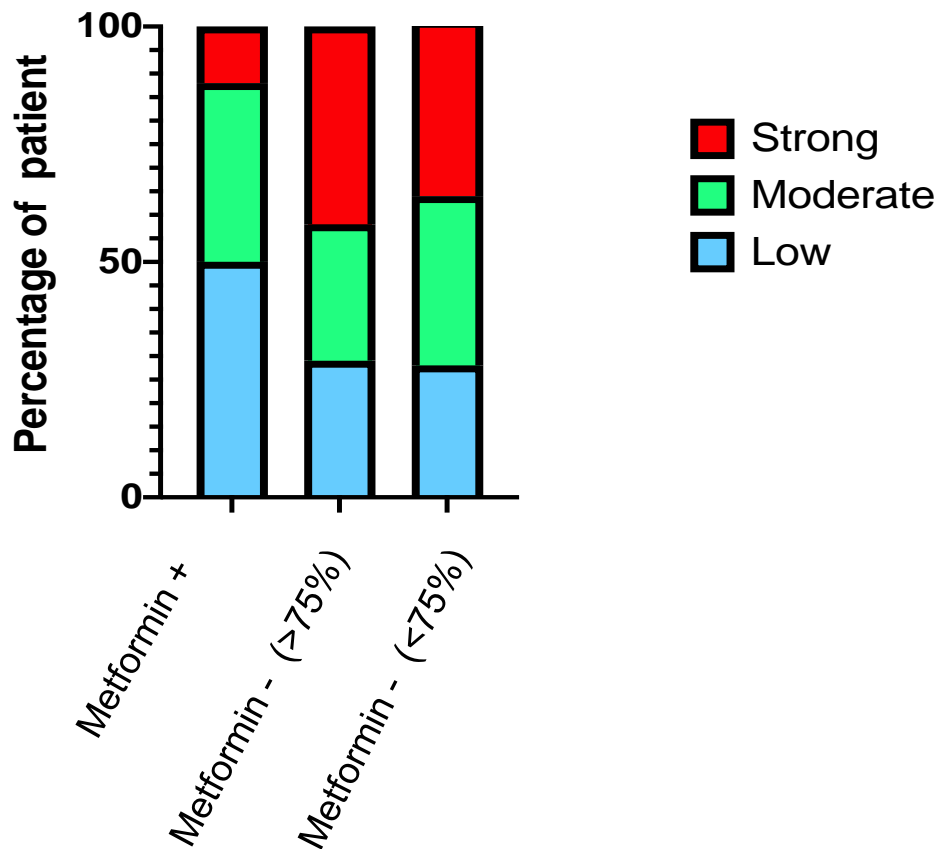
**H-Score of p-AMPK
in post-chemotherapy sample**



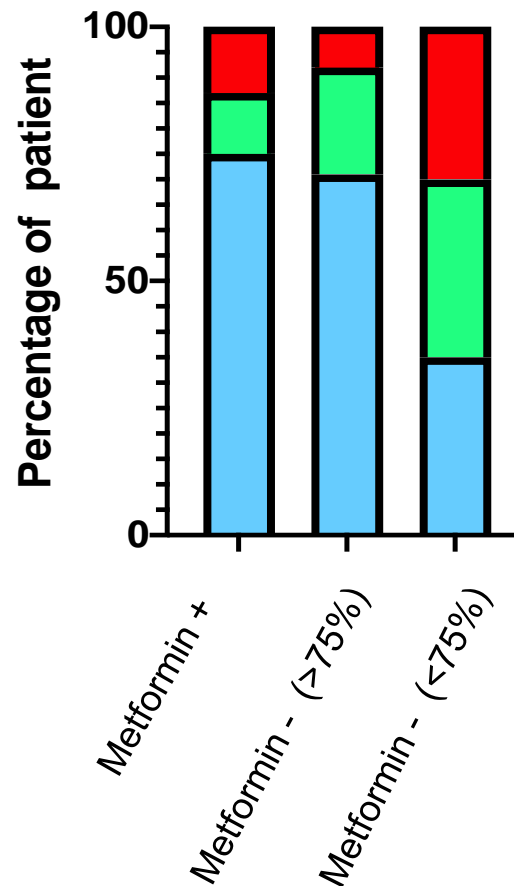
Increase of p-AMPK with chemotherapy in good responders

Higher baseline p-AMPK in Metformine USERS

H-Score of p-S6RP in prechemotherapy sample



H-Score of p-S6RP in postchemotherapy sample



Decrease of p-S6RP with chemotherapy in good responders

Lower baseline p-S6RP in Metformine USERS

Conclusions

1. Metformine USERS have less aggressive Bca

More Luminal A and B than Metformine NON USERS

2. Metformine USERS present higher reduction of tumor size with chemo

3. Downregulation of mTOR is associated with response to chemo

High p-AMPK

Low p-S6RP

Thank you for your attention