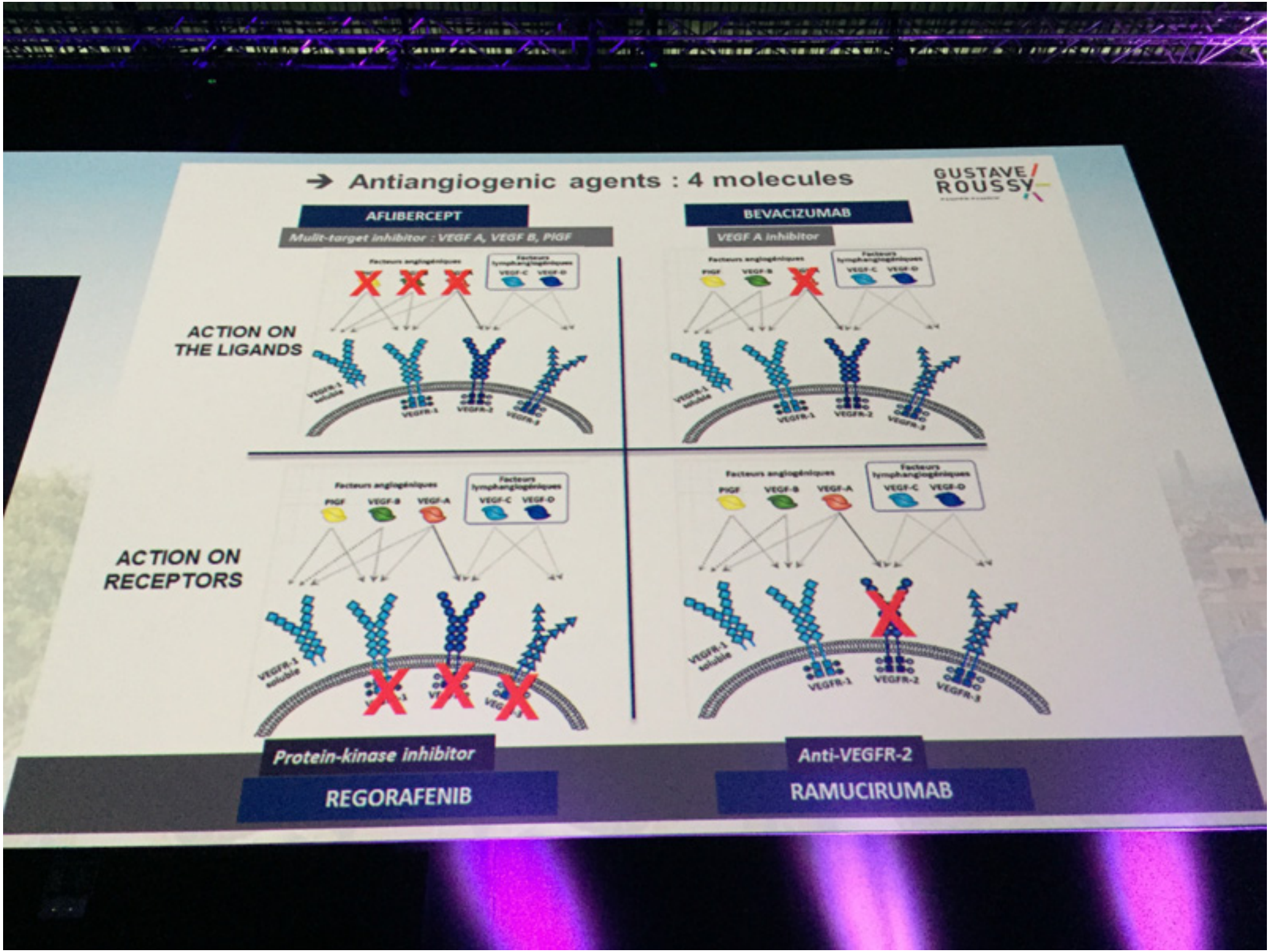
GUSTAVE ROUSSY

→ Biologics: Two main directions

1. *Continuous inhibition of angiogenesis*
   - *Possible in Ras wild type and mutated tumors*
2. *Continuous inhibition of EGFR pathway*
   - *Possible only in Ras wt tumors*

- *In other words:*


→ Antiangiogenic agents : 4 molecules
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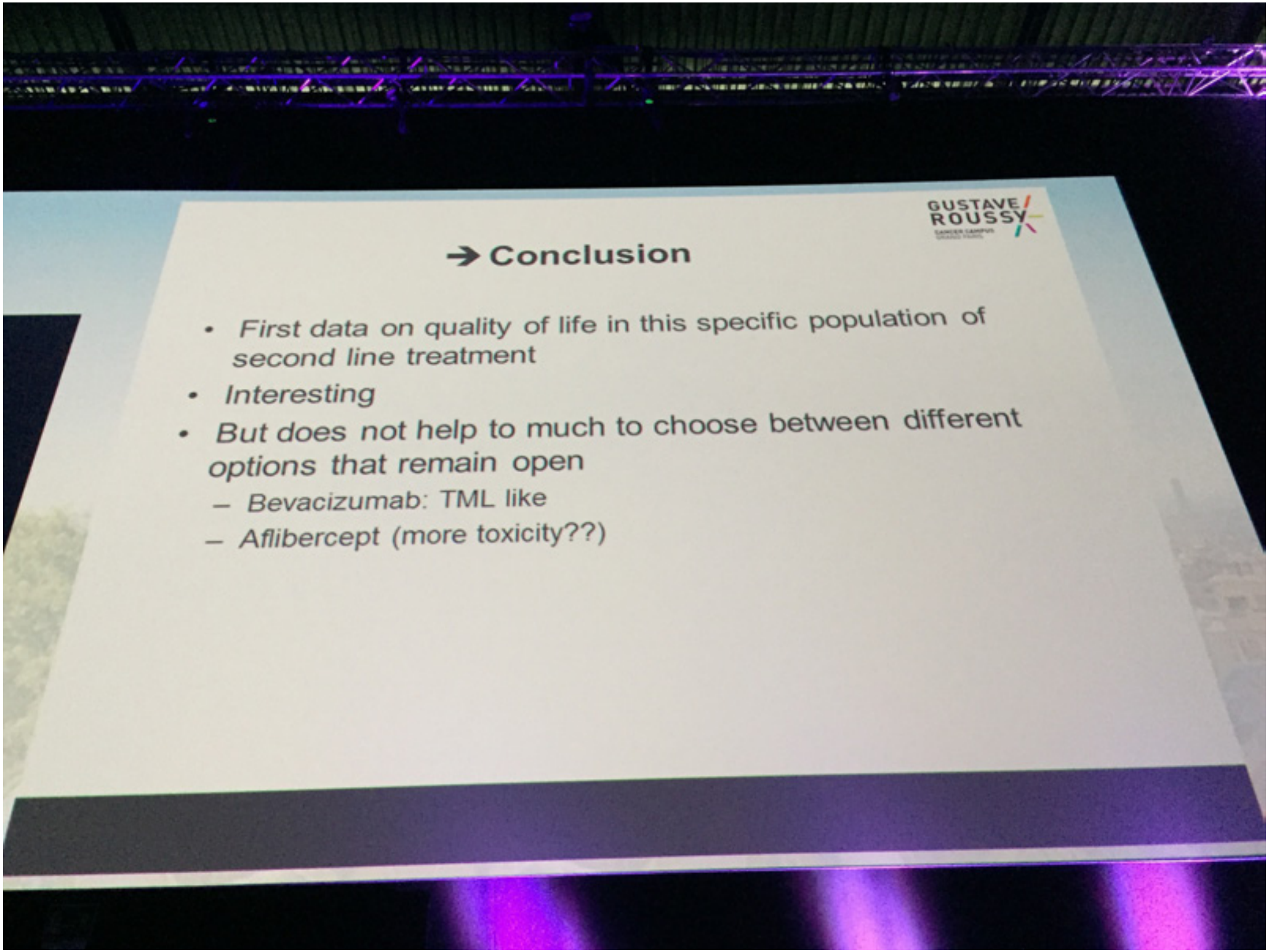
AFLIBERCEPT
Mulit-target inhibitor : VEGF A, VEGF B, PlGF
BEVACIZUMAB
VEGF A inhibitor
ACTION ON THE LIGANDS
ACTION ON RECEPTORS
Facteurs angiogéniques
Facteurs lymphangiogéniques
PlGF
VEGF-B
VEGF-A
VEGF-C
VEGF-D
VEGFR-1 soluble
VEGFR-1
VEGFR-2
VEGFR-3
Protein-kinase inhibitor
REGORAFENIB
Anti-VEGFR-2
RAMUCIRUMAB

→ Differences in toxicity??

	TML		VELOUR		RAISE	
	CT	CT + BEV	FOLFIRI	FOLFIRI + AFLI	FOLFIRI	FOLFIRI + RAMU
Neutropenia	13	16	29	37	23	38
Thrombopenia	?	?	2	3	1	3
Diarrhoea	8	10	8	19	10	11
Mucosal inf.	1	3	5	14	2	4
Infection	?	?	7	11	?	?
VTE	3	5	6	8	2	4
GI perforation	<1	2	<1	<1	<1	2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➔ Conclusion
• First data on quality of life in this specific population of second line treatment
• Interesting
• But does not help to much to choose between different options that remain open
– Bevacizumab: TML like
– Aflibercept (more toxicity??)

→ Biologics: The other direction

1. *Continuous inhibition of angiogenesis*
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2. *Continuous inhibition of EGFR pathway*
   - *Possible only in Ras wt tumors*

- *In other words:*

Ras wt:

Beva: TML
Afli: VELOUR
Ramu: RAISE

Cetux Ciardello

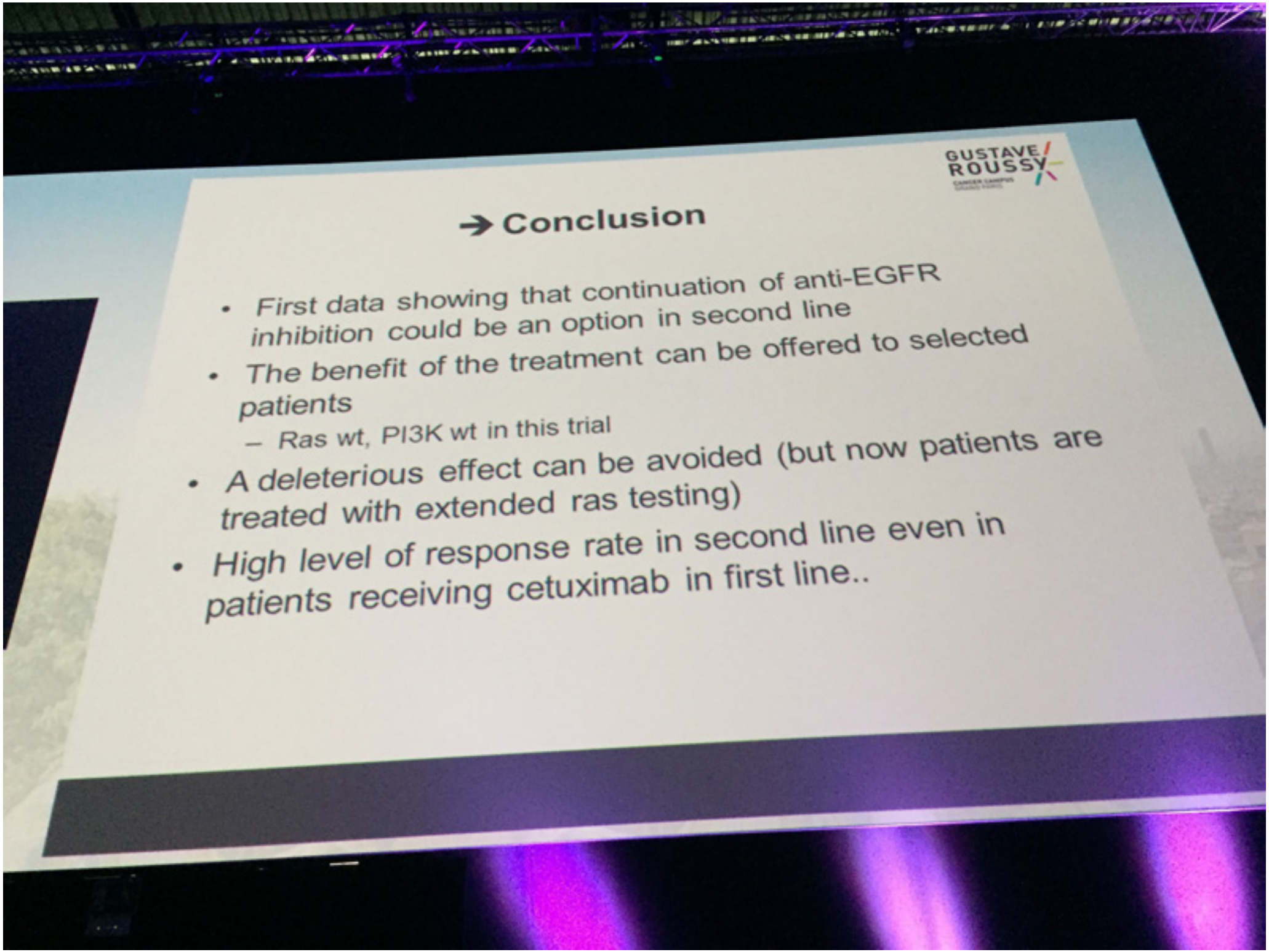
Ras mt:

Beva: TML
Afli: VELOUR
Ramu: RAISE

→ High rate of objective responses in second line?

	Giantonio		TML		VELOUR		RAISE	
	Folfox	+ bev	CT	+ bev	Folfiri	+ afli	Folfiri	+ ramu
ORR	9%	23%	4%	5%	11%	19%	12%	13%

	EPIC		181		This study	
	irinotecan	+ cetux	Folfiri	+ pani	Folfox	+ cetux
ORR	4%	16%	10%	36%	9%	26%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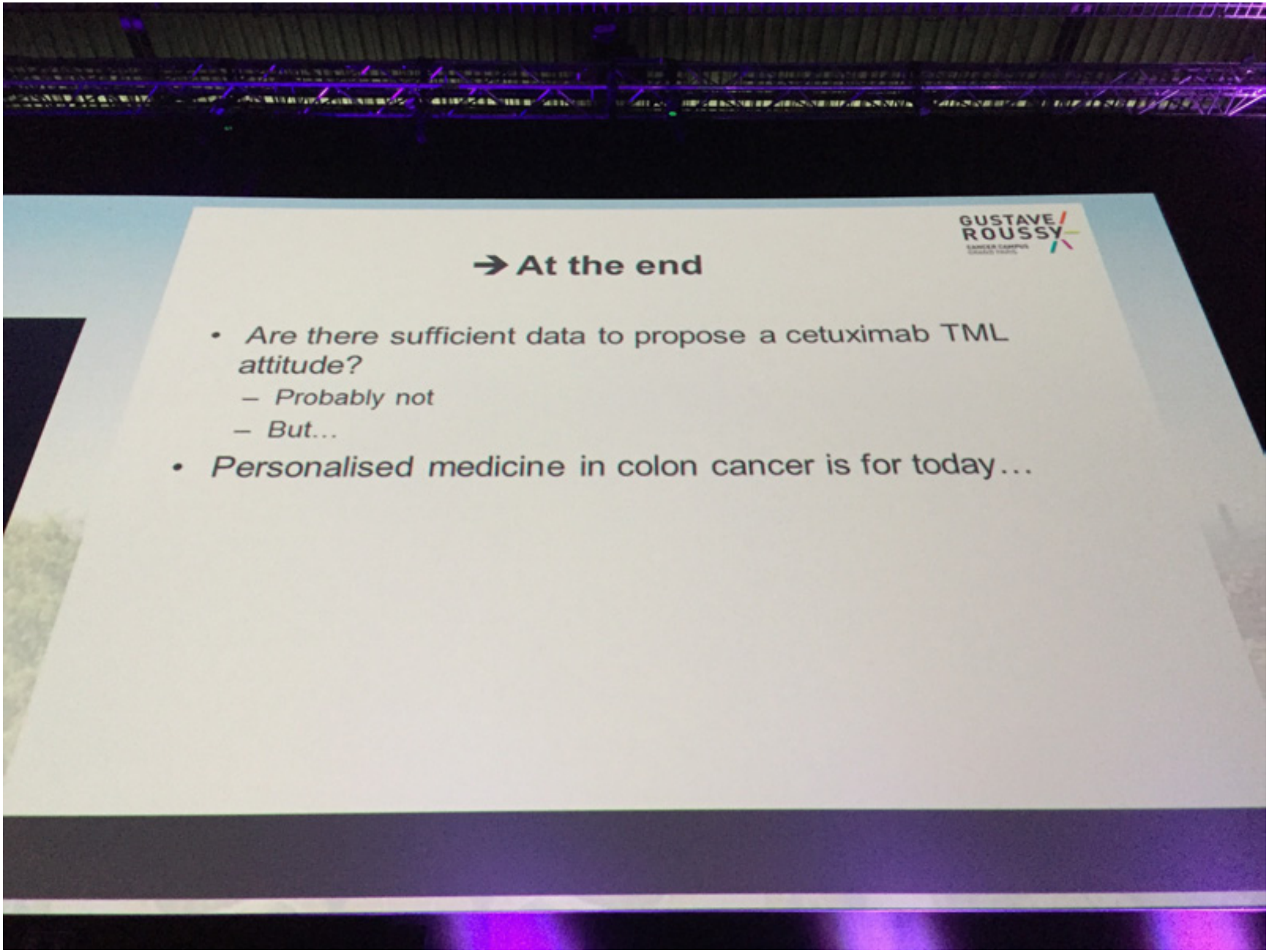
CANCER CAMPUS
➔ Conclusion
First data showing that continuation of anti-EGFR inhibition could be an option in second line
The benefit of the treatment can be offered to selected patients
– Ras wt, PI3K wt in this trial
A deleterious effect can be avoided (but now patients are treated with extended ras testing)
High level of response rate in second line even in patients receiving cetuximab in first line..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➔ At the end
• Are there sufficient data to propose a cetuximab TML attitude?
– Probably not
– But…
• Personalised medicine in colon cancer is for today…

→ Biologics: Two main directions

1. *Continuous inhibition of angiogenesis*
   - *Possible in Ras wild type and mutated tumors*
2. *Continuous inhibition of EGFR pathway*
   - ***The best choice in the future for very selected tumors??***

- *In other words:*