



3^{ème} journée FILFOIE

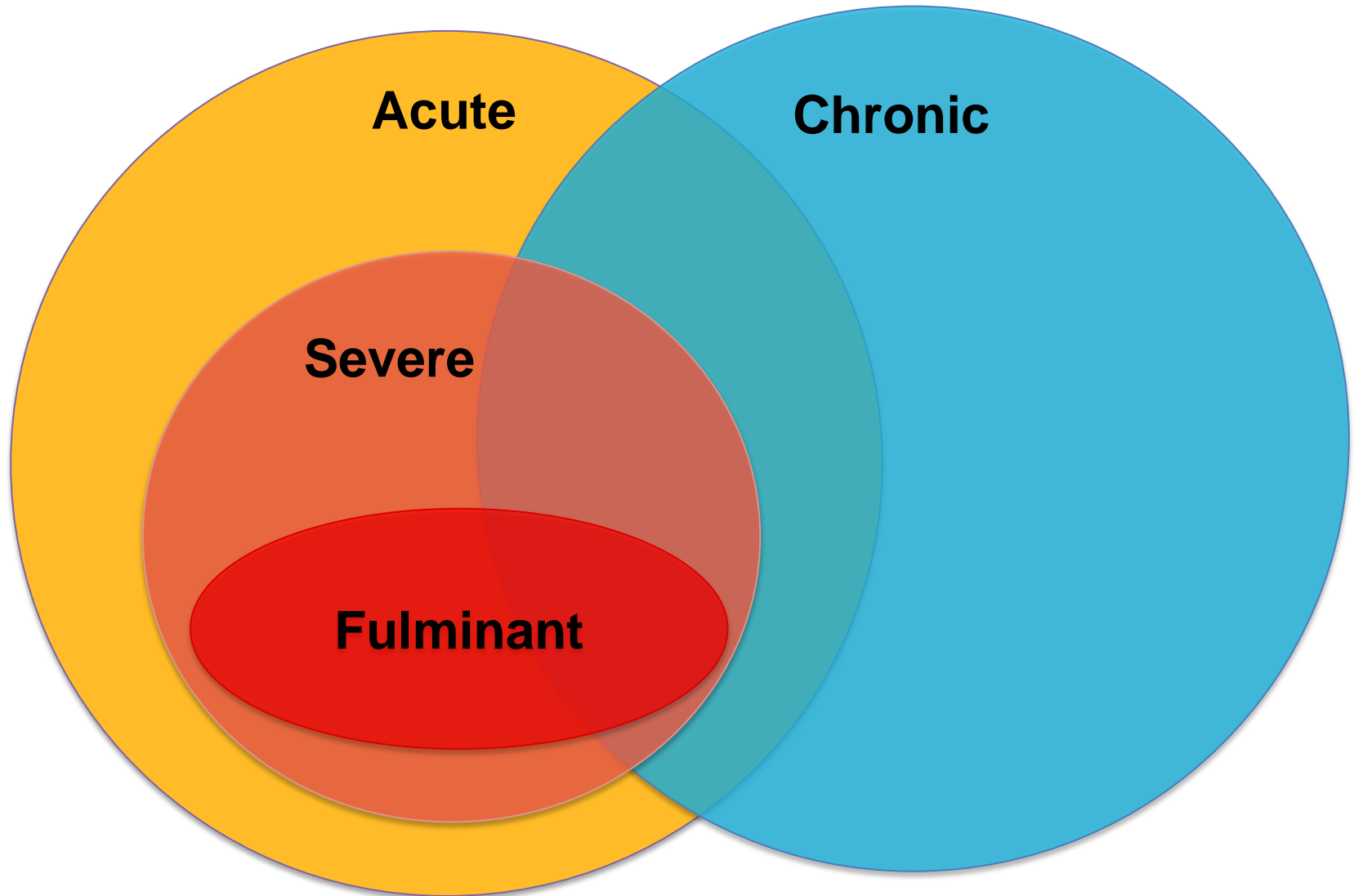
Étude SURFASA : Survie et facteurs pronostiques dans l'hépatite autoimmune aiguë sévère

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Différentes spectrum des HAI



Le rôle des corticoïdes dans les HAI aigue sévère est encore controversé

Uselessness of corticosteroids in severe and fulminant forms

Ichai, Liver Transpl 2007

12/16 (75%)
treated patients



10/12 (83%)
liver
transplantation



The role of corticosteroids in modifying outcome

Yeoman, J Hepatol 2015

23/32 (75%)
treated patients



10/23 (43%)
liver
transplantation

De Martin, J Hepatol 2015

But de l'étude

Chez les patients ayant un hépatite auto-immune aigue sévère (AS-AIH) évaluer:

- Les caractéristiques de la population
- La survie globale
- La décision du traitement par corticoïdes
- La réponse aux corticoïdes

Méthods

- Étude multicentrique rétrospective française: 23 centres
- Entre Jan 2009 et Fev 2016
- Le diagnostic AS-AIH défini par:
 1. Absence ATCD d'AIH
 2. International Autoimmune Hepatitis Group (IAIHG) score "definite" ou "probable"
 3. INR \geq 1.5 et/ou bilirubine totale $>$ 200 $\mu\text{mol/L}$
 4. Diagnostic histologique d'AIH
- Critères d'exclusion: ATCD d'hépatopathie chronique et autre cause d'hépatite aigue sévère

Caractéristiques de la population générale

| | N=128 |
|---|-----------------|
| Age, year | 52 [39-62] |
| Gender, female | 92 (72) |
| Extra hepatic autoimmune disease | 31 (29) |
| Hepatic encephalopathy (grade \geq 1) | 12 (10) |
| Clinical ascites | 19 (17) |
| AST, IU/L | 1105 [672-1644] |
| ALT, IU/L | 969 [585-1580] |
| GGT, IU/L | 157 [85-295] |
| Total bilirubin, μ mol/L | 259 [197-400] |
| INR | 1.8 [1.6-2.6] |
| Creatinine, μ mol/L | 62 [54-79] |
| MELD | 25 [21-28] |

The continuous variables are expressed using median [range IQR 1st and 3rd]. The qualitative variables are expressed using number (%).

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Caractéristiques de la population générale

| | N=128 |
|-----------------------|-------------------|
| Albumin, g/dL | 28 [24-32] |
| Platelets, G/L | 163 [120-238] |
| IgG, g/L | 20 [15-33] |
| ANA > 1:80 | 63 (61) |
| ASMA > 1:80 | 53 (49) |
| Fibrosis stage F0-1* | 49 (48) |
| Fibrosis stage F2-F3* | 32 (31) |
| Fibrosis stage F4* | 22 (21) |
| Infection occurrence | 32 (27) |
| ICU admission | 52 (45) |
| Follow-up, months | 29 [14-52] |

*METAVIR score

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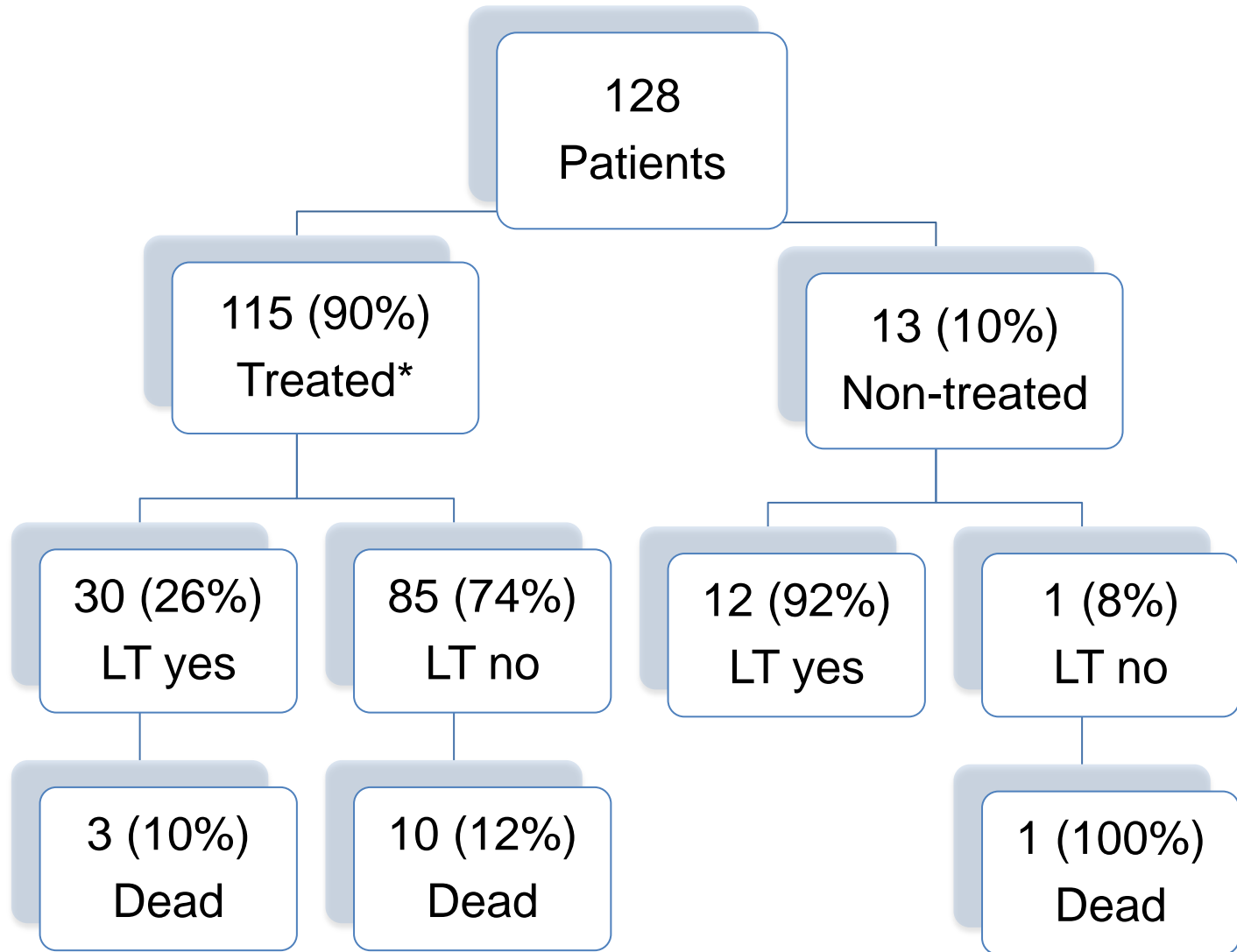
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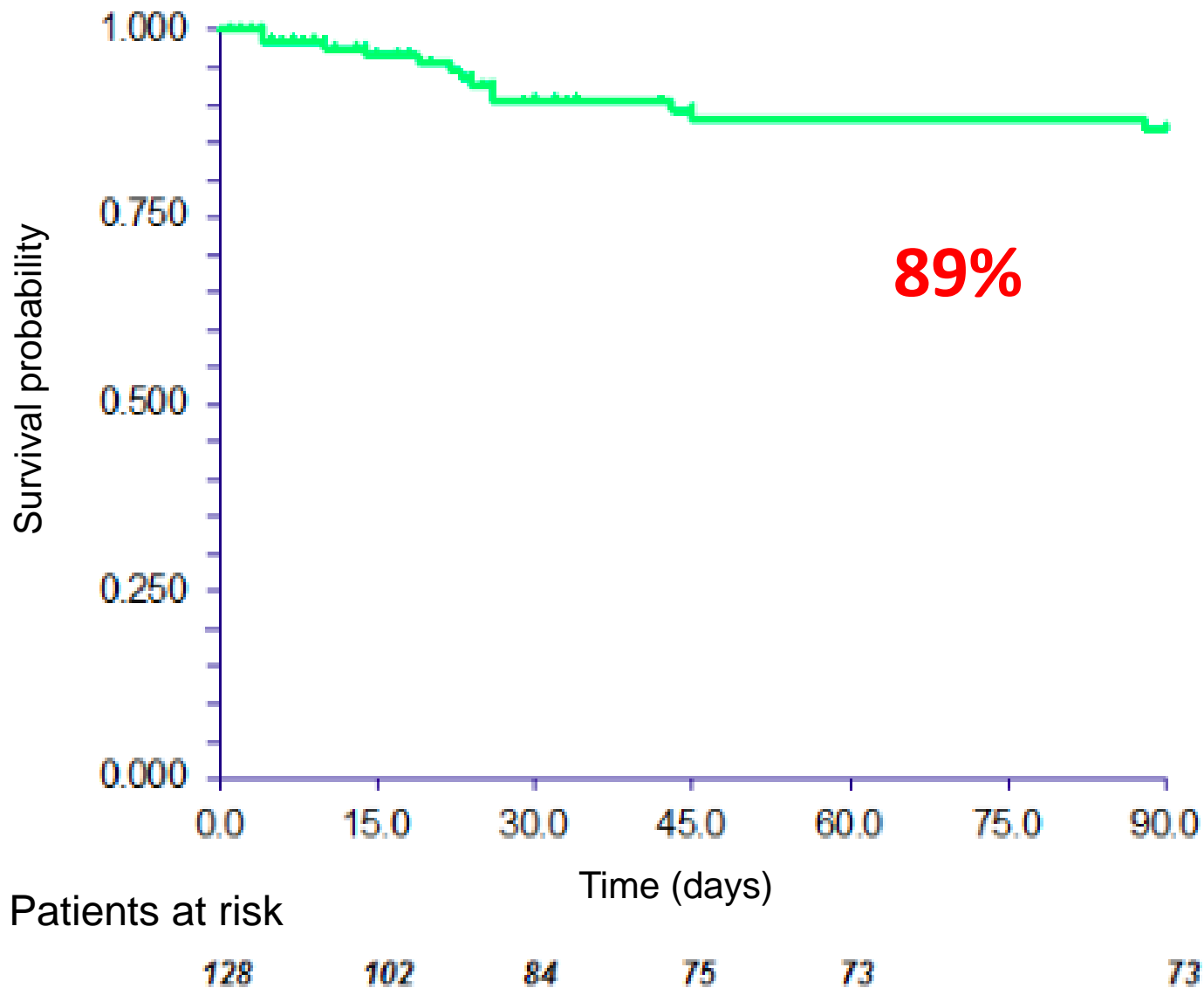
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Prise en charge et résultats



*Corticosteroid therapy

Survie globale à 90 jours



Facteurs prédictives de survie globale

| | N=114 alive | N=14 dead | p |
|--|----------------------|---------------------|---------------|
| Age, years | 49 [38-61] | 61 [56-79] | 0.0003 |
| Gender, female | 85 (75) | 7 (50) | 0.0648 |
| HE | 14 (14) | 2 (15) | 1.0000 |
| Clinical ascites | 15 (13) | 4 (29) | 0.2280 |
| ALT, IU/L | 996 [41-1580] | 750 [357-1818] | 0.4532 |
| Total bilirubin, µmol/L | 256 [197-376] | 352 [204-463] | 0.3244 |
| INR | 1.8 [1.6-2.6] | 2.2 [1.8-2.6] | 0.0847 |
| Creatinine, µmol/L | 62 [52-75] | 73 [61-81] | 0.0684 |
| MELD | 25 [21-28] | 26 [24-33] | 0.3395 |
| Platelets, G/L | 170 [127-248] | 130 [75-147] | 0.0076 |
| Infection occurrence | 26 (23) | 6 (43) | 0.1398 |
| Corticosteroid therapy | 102 (89) | 13 (93) | 1.0000 |
| Interval admission-corticosteroids, days | 5 [2-10] | 9 [3-11] | 0.4923 |

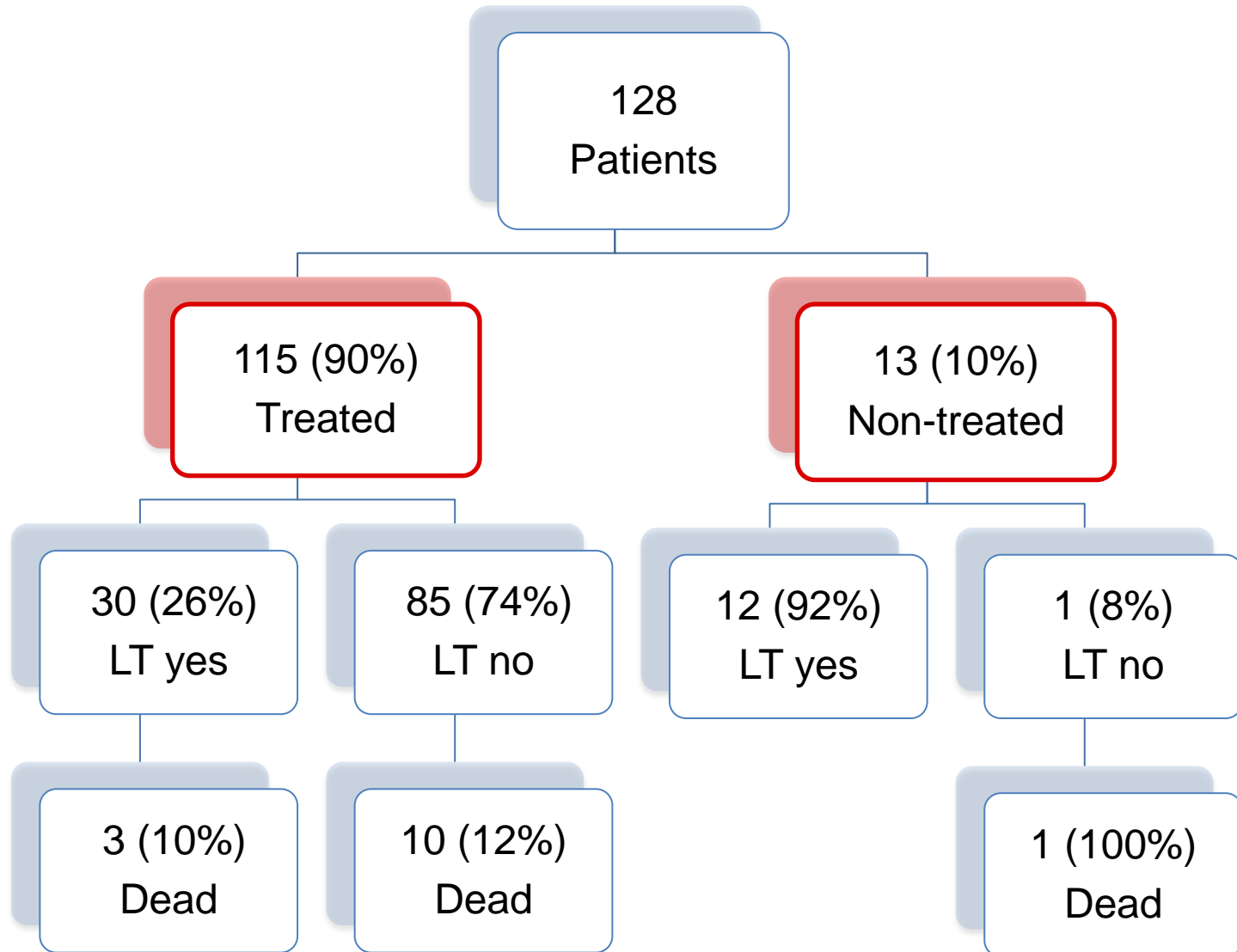
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Facteurs prédictives de survie globale

| | N=114 alive | N=14 dead | p | OR | 95% CI | p |
|--|----------------------|---------------------|---------------|--------------|--------------------|---------------|
| Age, years | 49 [38-61] | 61 [56-79] | 0.0003 | 1.087 | 1.028-1.149 | 0.0035 |
| Gender, female | 85 (75) | 7 (50) | 0.0648 | 0.183 | 0.039-0.868 | 0.0325 |
| HE | 14 (14) | 2 (15) | 1.0000 | | | |
| Clinical ascites | 15 (13) | 4 (29) | 0.2280 | | | |
| ALT, IU/L | 996 [41-1580] | 750 [357-1818] | 0.4532 | | | |
| Total bilirubin, µmol/L | 256 [197-376] | 352 [204-463] | 0.3244 | | | |
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| Creatinine, µmol/L | 62 [52-75] | 73 [61-81] | 0.0684 | | | |
| MELD | 25 [21-28] | 26 [24-33] | 0.3395 | | | |
| Platelets, G/L | 170 [127-248] | 130 [75-147] | 0.0076 | 0.986 | 0.974-0.999 | 0.0326 |
| Infection occurrence | 26 (23) | 6 (43) | 0.1398 | | | |
| Corticosteroid therapy | 102 (89) | 13 (93) | 1.0000 | | | |
| Interval admission-corticosteroids, days | 5 [2-10] | 9 [3-11] | 0.4923 | | | |

The continuous variables are expressed using median [range IQR 1st and 3rd]. The qualitative variables are expressed using number (%).

Comment la décision de l'introduction des corticoïdes a été prise?

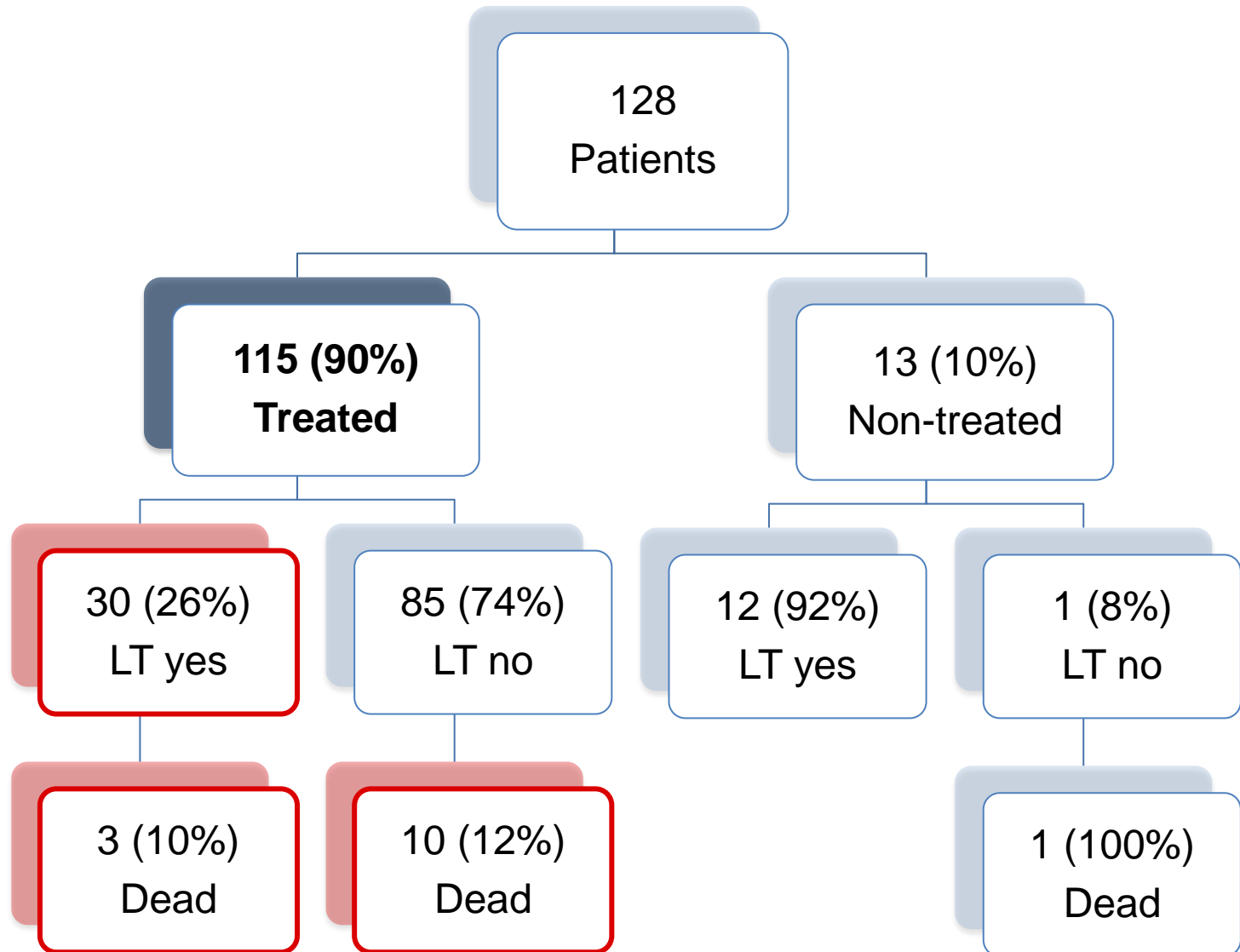


Patients traités par corticoïdes vs non traités

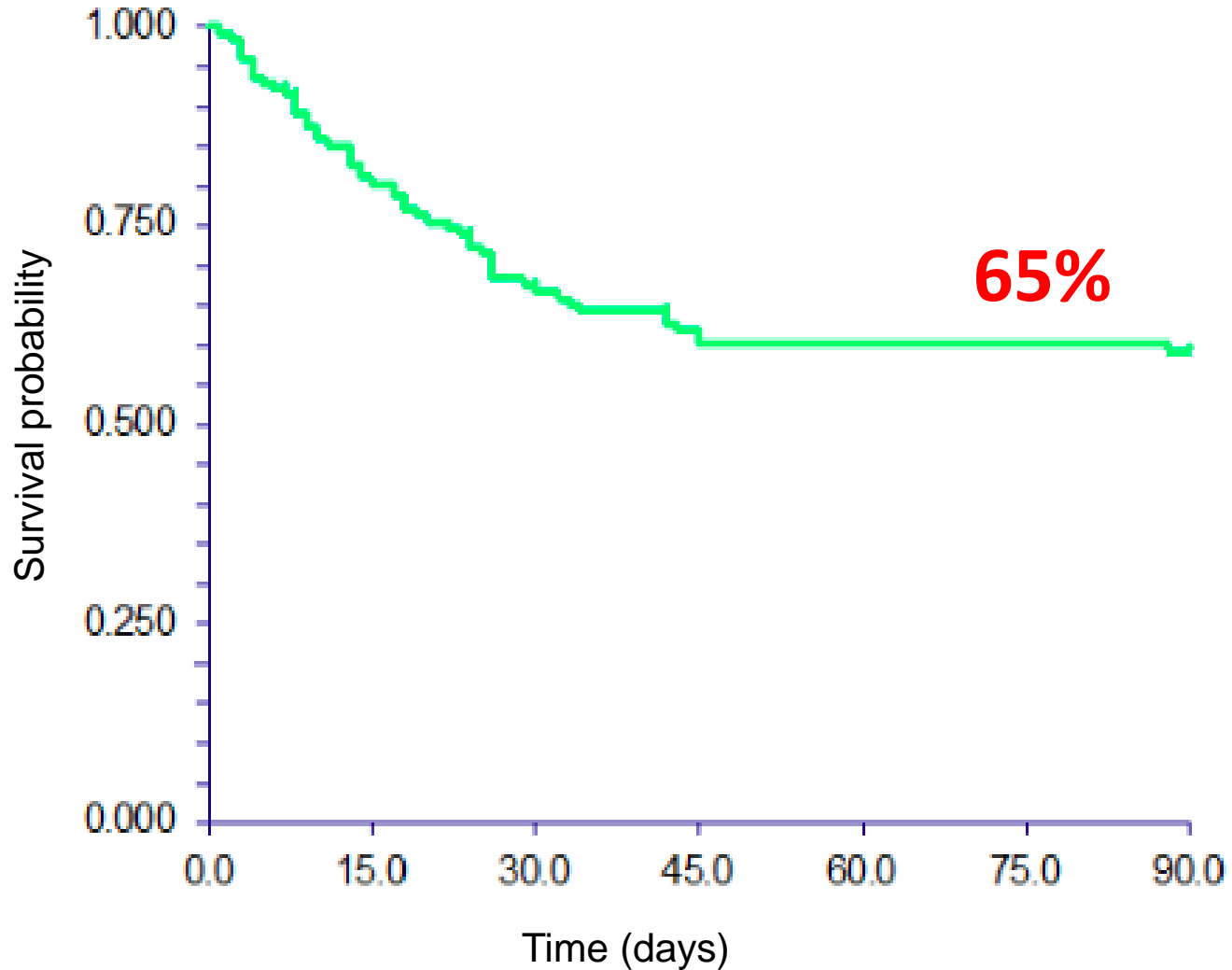
| | Treated N=115 | Non-treated N=13 | p |
|-------------------------------|--------------------------|-----------------------------|------------------|
| Age, years | 53 [39-63] | 51 [39-56] | ns |
| Gender, female | 84 (73) | 8 (61) | ns |
| Hepatic encephalopathy | 6 (5) | 12 (92) | <.0001 |
| Clinical ascites | 14 (12) | 5 (38) | 0.0421 |
| ALT, IU/L | 996 [549-1548] | 843 [641-1834] | ns |
| Total bilirubin, µmol/L | 259 [194-388] | 256 [220-403] | ns |
| INR | 1.8 [1.6-2.2] | 3.4 [2.6-5.4] | 0.0003 |
| Creatinine, µmol/L | 61 [52-75] | 79 [66-139] | 0.0113 |
| MELD | 24 [21-27] | 34 [28-40] | 0.0007 |

The continuous variables are expressed using median [range IQR 1st and 3rd]. The qualitative variables are expressed using number (%).

Quels sont les facteurs prédictives de la réponse aux corticoïdes défini comme survie sans TH?



Réponse aux corticoïdes à 90 jours



Facteurs prédictives de réponse aux corticoïdes

| | Responders* N= 77 | Non Responders* N= 36 | p |
|---------------------------------------|------------------------------|----------------------------------|------------------|
| Age, years | 52 [39-63] | 54 [41-61] | 0.9803 |
| Gender, female | 58 (75) | 24 (67) | 0.3365 |
| HE | 1 (1) | 5 (14) | 0.0185 |
| ALT, IU/L | 784 [407-1120] | 699 [408-1124] | 0.9067 |
| Total bilirubin, µmol/L | 272 [207-386] | 346 [265-414] | 0.0803 |
| INR | 1.6 [1.4-2] | 2.7 [2-3.6] | <.0001 |
| Creatinine, µmol/L | 59 [52-72] | 63 [50-71] | 0.9374 |
| MELD | 22 [21-24] | 28 [26-32] | <.0001 |
| Platelets, G/L | 202 [145-275] | 130 [81-196] | 0.0007 |
| Infection | 13 (19) | 13 (36) | 0.0468 |
| Admission corticosteroids, days | 7 [3-10] | 4 [2-9] | 0.4058 |
| Fibrosis stage 0-1/ 2-3/ 4 | 29(43)/27(40)/12(18) | 14(56)/3(12)/8(32) | 0.0333 |

* 2 patients were excluded, 1 dead and 1 LT before day 3 of corticosteroid therapy

The continuous variables are expressed using median [range IQR 1st and 3rd]. The qualitative variables are expressed using number (%).

Facteurs prédictives de réponse aux corticoïdes

| | Responders* N= 77 | Non Responders* N= 36 | p | OR | 95%CI | p |
|---------------------------------------|-----------------------------|---------------------------|------------------|--------------|--------------------|------------------|
| Age, years | 52 [39-63] | 54 [41-61] | 0.9803 | | | |
| Gender, female | 58 (75) | 24 (67) | 0.3365 | | | |
| HE | 1 (1) | 5 (14) | 0.0185 | | | |
| ALT, IU/L | 784 [407-1120] | 699 [408-1124] | 0.9067 | | | |
| Total bilirubin, µmol/L | 272 [207-386] | 346 [265-414] | 0.0803 | | | |
| INR | 1.6 [1.4-2] | 2.7 [2-3.6] | <.0001 | 8.533 | 3.270-22.26 | <.0001 |
| Creatinine, µmol/L | 59 [52-72] | 63 [50-71] | 0.9374 | | | |
| MELD | 22 [21-24] | 28 [26-32] | <.0001 | | | |
| Platelets, G/L | 202 [145-275] | 130 [81-196] | 0.0007 | | | |
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* 2 patients were excluded, 1 dead and 1 LT before day 3 of corticosteroid therapy

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Facteurs prédictives de réponse aux corticoïdes

| | Responders N=77 | Non Responders N=36 | p |
|--|----------------------------|------------------------------------|------------------|
| Delta ALT d3-d0 | -132 [-391/-45] | -89 [-317/-13] | 0.3573 |
| Delta Total bilirubin d3-d0 | -51 [-85/-14] | 17 [-19/64] | <.0001 |
| Delta INR d3-d0 | 0 [-0.16/0.0] | 0 [0.0/0.2] | 0.0162 |
| Delta MELD d3-d0 | -0.9 [-2.2/0.07] | 0.3 [-0.43-1.5] | 0.0015 |
| Delta ALT d7-d0 | -278 [-577/-88] | -186[-482/-18] | 0.3841 |
| Delta Total bilirubin d7-d0 | -98 [-140/-22] | 6.5 [-90/117] | 0.0072 |
| Delta INR d7-d0 | -0.2 [-0.3/0.0] | 0.2 [-0.2/0.4] | 0.0004 |
| Delta MELD d7-d0 | -2.8 [-4.13/-1] | 0.0 [-1.0/2.8] | 0.0004 |

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| Delta ALT d3-d0 | -132 [-391/-45] | -89 [-317/-13] | 0.3573 | | | |
| Delta Total bilirubin d3-d0 | -51 [-85/-14] | 17 [-19/64] | <.0001 | 1.017 | 1.001-1.034 | 0.0365 |
| Delta INR d3-d0 | 0 [-0.16/0.0] | 0 [0.0/0.2] | 0.0162 | | | |
| Delta MELD d3-d0 | -0.9 [-2.2/0.07] | 0.3 [-0.43-1.5] | 0.0015 | | | |
| Delta ALT d7-d0 | -278 [-577/-88] | -186[-482/-18] | 0.3841 | | | |
| Delta Total bilirubin d7-d0 | -98 [-140/-22] | 6.5 [-90/117] | 0.0072 | 1.004 | 1.000-1.008 | 0.0485 |
| Delta INR d7-d0 | -0.2 [-0.3/0.0] | 0.2 [-0.2/0.4] | 0.0004 | | | |
| Delta MELD d7-d0 | -2.8 [-4.13/-1] | 0.0 [-1.0/2.8] | 0.0004 | | | |

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Conclusion

- La survie à 90 jours chez les patients ayant une hépatite auto-immune aiguë sévère est de 89%
- Les facteurs prédictives de la survie globale sont l'âge, le genre féminine et le taux de plaquettes
- Les patients non traités par corticoïdes avaient les critères de greffe de l'admission et 92% ont été transplantés
- Parmi les patients traités par corticoïdes, la TH et la mortalité sont de 26% et 12% respectivement
- La réponse aux corticoïdes est de 65% et les facteurs prédictives de la réponse sont **l'INR, l'amélioration de la bilirubine totale à 3 jours et à 7 jours de le début du traitement**
- Le prochain objectif est la création d'un score avec ces variables identifiant un règle d'arrêt des corticoïdes.

Remerciements

