

# LABQUALITY

External Quality Assessment Scheme

## Histopathology, virtual microscopy: Lymphohematopoietic pathology Round 1, 2023

### Specimens

Please find enclosed 7 specimens as cases with virtual microscopy images. Images of immunohistochemical stainings are included in some cases.

### Background information

The whole specimen slide has been scanned. The samples have been fixed with formalin and stained with haematoxylin and eosin (HE). Patient's age, sex and available data of clinical history are given.

### Parameters

The participants are requested to give an interpretation comparable to normal clinical situation, i.e. the diagnosis and there is also a free text field for comments. Responses from individual pathologists are requested instead of responses based on group consensus. It is important to take into account that this external quality assessment scheme does not evaluate histological examination as a medical consultation.

### Using a web browser

Please use Mozilla Firefox, Google Chrome or Microsoft Edge as a web browser when using LabScala. Do not use Internet Explorer. If you have problems viewing the slides and you see the Aiforia logo only but no slides, please ask your IT department to allow access to webpage <http://cloud.aiforia.com>.

### Result reporting

Please enter the results and methods via LabScala ([www.labscala.com](http://www.labscala.com)). Every case has its own sheet. There is one virtual microscopy image per case. The images will open into a new window. If you want to send more than one result per case, press + sign on blue bar, and a new set of questions opens. Results will not be hidden. In order to separate your five results, give each a respondent name. If respondents are not supposed to see what others have replied, collect results first on paper and enter to LabScala at the same time. Remember to save after every case.

Save as draft if you have many respondents. Save as final if you are the only or final respondent. Move to next case by choosing Next. After you have filled all the results and saved them as final, send the results to Labquality. With one order it is possible to return max. five results/case.

### CASES

#### Case 1 (S001: LQ778123011)

A 77-year-old man. Laparoscopic lymph node biopsy for suspected lymphoma.

#### Case 2 (S002: LQ778123012)

A 69-year-old woman. 2012 left breast cancer, resection, axillary evacuation, chemotherapy, hormonal therapy and radiotherapy. Enlarged lymph nodes on the left side of the neck in the control ultrasound, the largest being 33 x 13 mm in size. A lymph node sample from the neck.

2023-03-28

### INSTRUCTIONS

Product no. 6542  
LQ778123011-017/F1  
Subcontracting: Digital image services

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The results should be reported no later than **May 1, 2023.**

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### Inquiries

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**Case 3** (S003: LQ778123013)

A 77-year-old man. Hospitalized due to shortness of breath, pleural fluid. Large number of prominent lymph nodes on both sides in the armpits, neck, clavicles and groin in the CT examination. Large spleen, ad 21cm, with non-specific lesion in the lateral part. A lymph node sample.

**Case 4** (S004: LQ778123014)

86-year-old man, hypertension, MCC, 2010 myocardial infarction, when PCI + stenting. Symptoms of infection for 2 weeks, despite antibiotic treatment, inflammation values persisted high, focus of infection unclear, liver chemistry elevated. On the upper body a vague, purplish skin change with slight ring-like formations, no ulcers, no itching. Vasculitis, exanthema consistent with borrelia, infection/drug?

**Case 5** (S005: LQ778123015)

A 76-year-old woman. Weight loss, loss of appetite. A carcinoma-like area in the ventricle on the small curvature, hard for biopsy forceps. Sample 1 normal duodenum, sample 2 normal antrum and samples 3 from the suspected carcinoma.

**Case 6** (S006: LQ778123016)

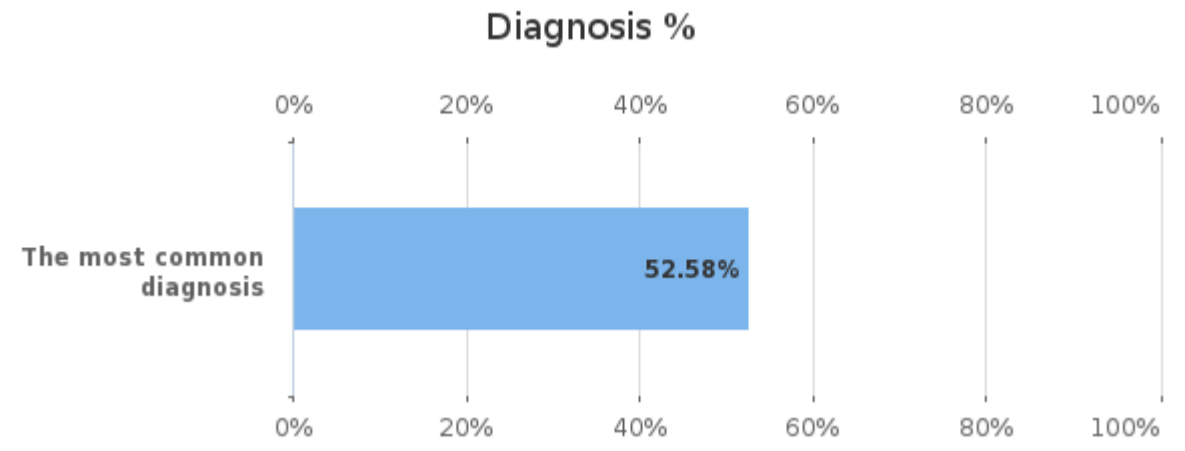
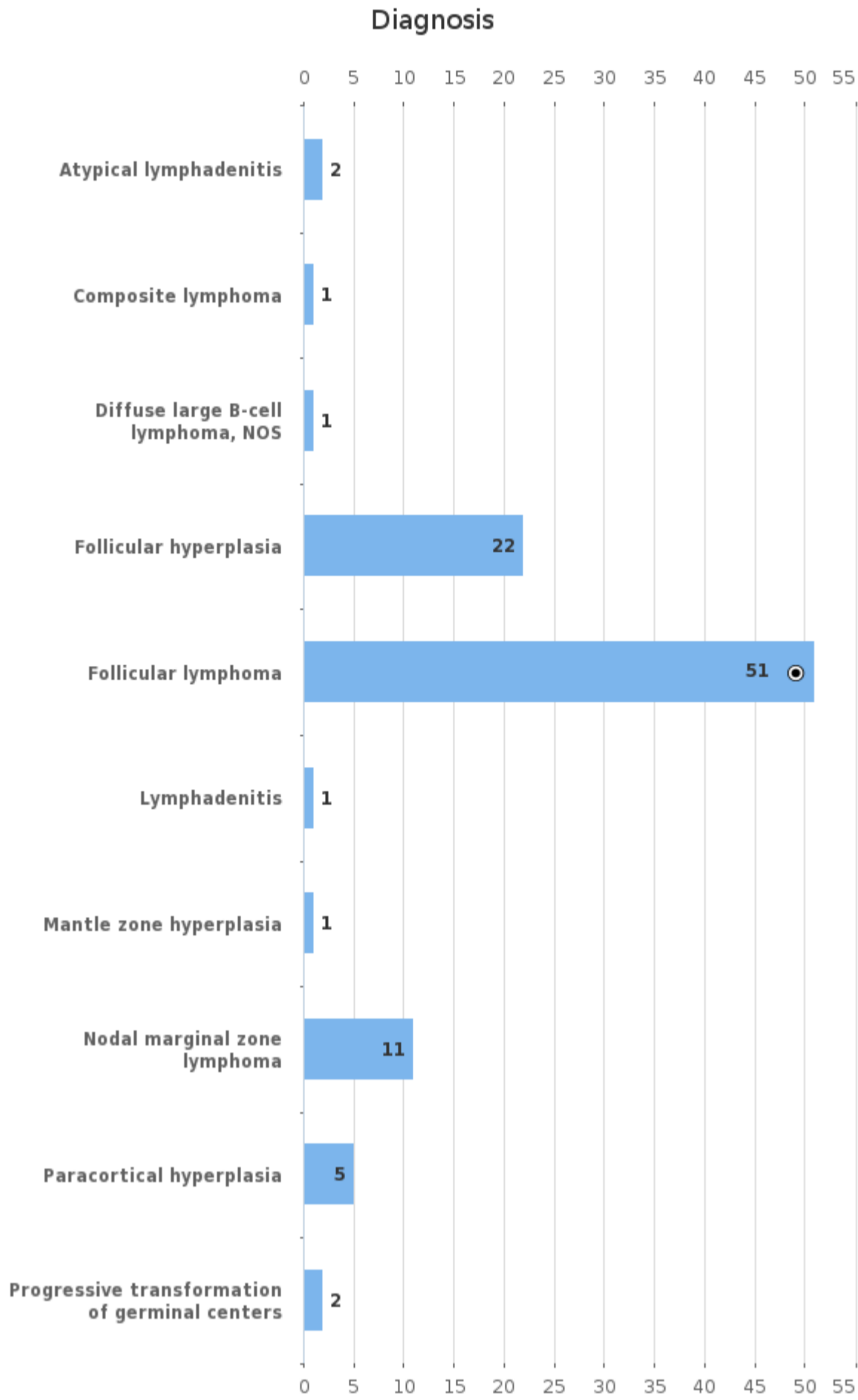
A generally healthy 16 years old boy. A sore throat and enlarged lymph nodes. The tonsils fill the entire oropharynx, emergency tonsillectomy performed.

**Case 7** (S007: LQ778123017)

A 43-year-old man. A tumor on the surface of the ileum, approximately 2 x 4 cm in size, was found to be the cause of intestinal bleeding. Only a small ulceration on the mucosa. Dozens of similar smaller tumors is seen all over the surface of the small intestine, in the mesentery and peritoneum. A sample taken from the surface of the proximal small intestine.

Round	No of participants	No of responded participants	Response percentage %
Histopathology, virtual microscopy, March, 1-2023	96	85	88.54%

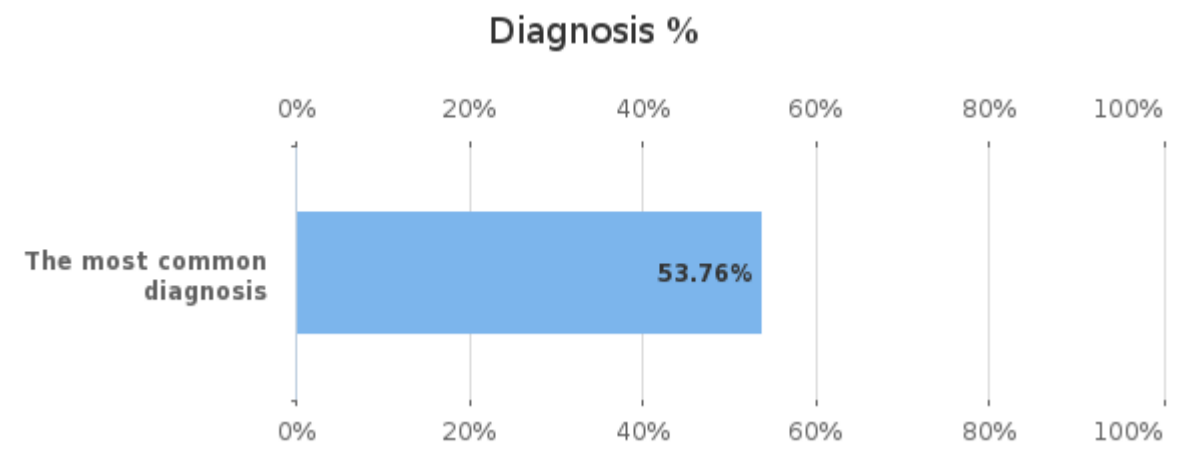
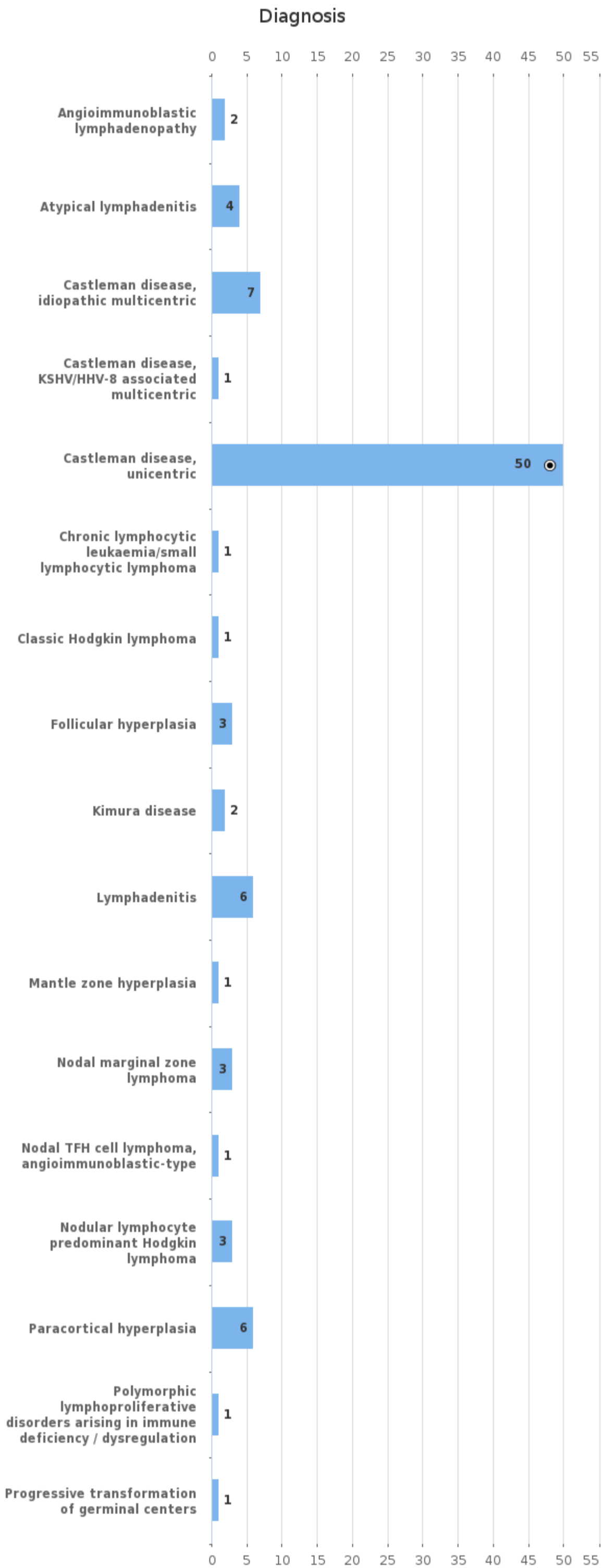
Case 1 | Diagnosis | P.K., E.L.



Diagnosis	n
Atypical lymphadenitis	2
Composite lymphoma	1
Diffuse large B-cell lymphoma, NOS	1
Follicular hyperplasia	22
Follicular lymphoma	51
Lymphadenitis	1
Mantle zone hyperplasia	1
Nodal marginal zone lymphoma	11
Paracortical hyperplasia	5
Progressive transformation of germinal centers	2
<b>Total</b>	<b>97</b>

Agreement percentage of the responses	%
The most common diagnosis	52.58

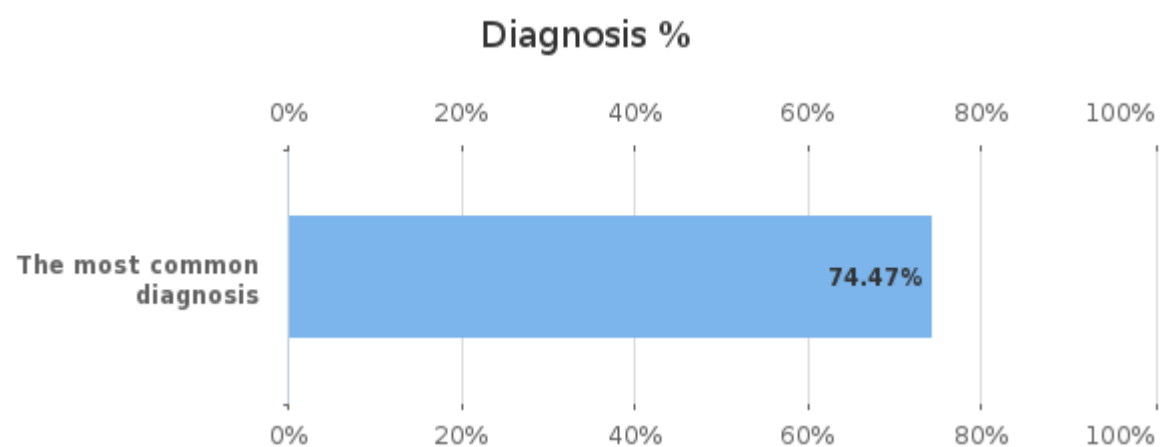
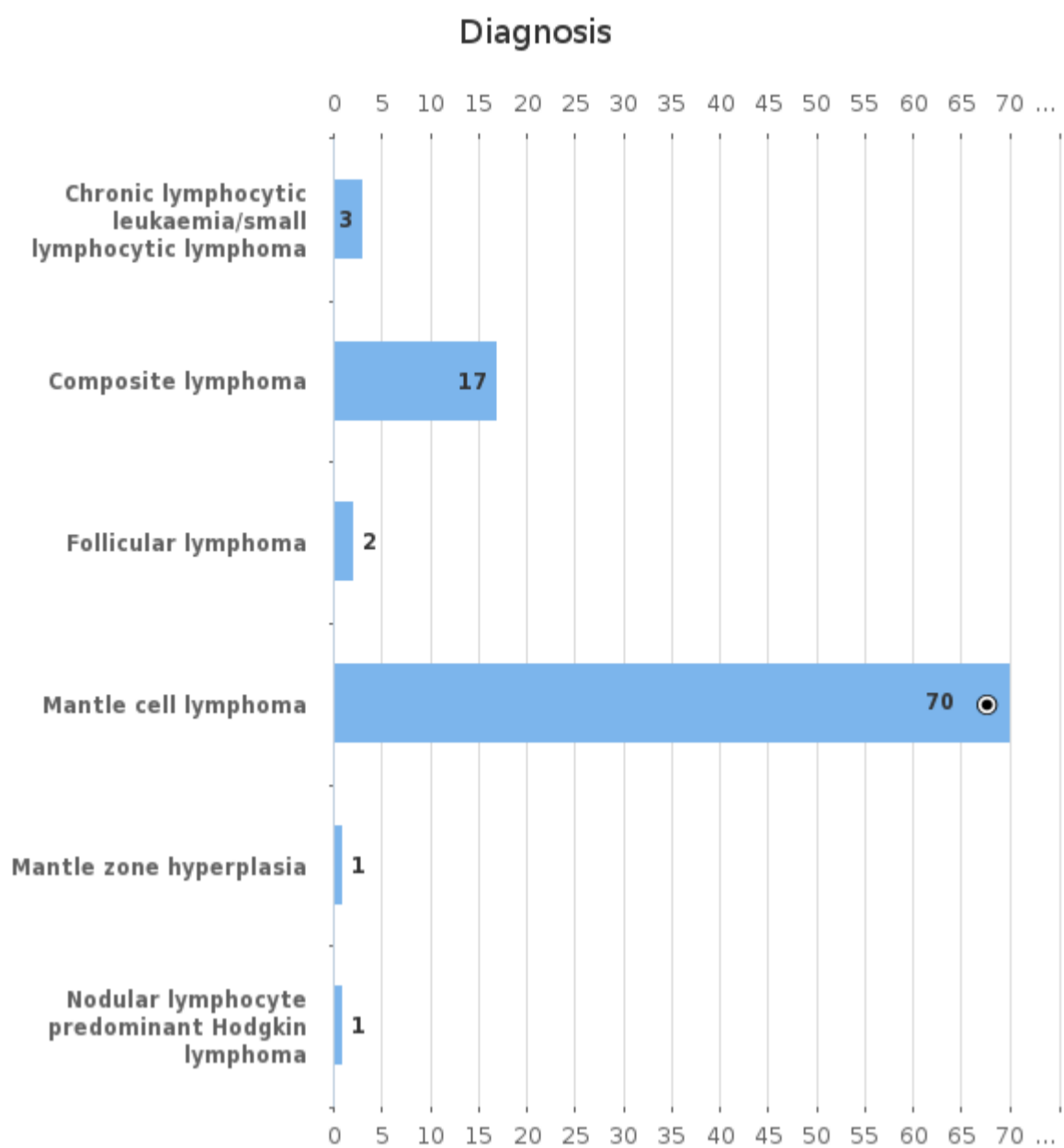
Case 2 | Diagnosis | P.K., E.L.



Diagnosis	n	Agreement percentage of the responses	%
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Angioimmunoblastic lymphadenopathy	2	The most common diagnosis	53.76
Atypical lymphadenitis	4		
Castleman disease, idiopathic multicentric	7		
Castleman disease, KSHV/HHV-8 associated multicentric	1		
Castleman disease, unicentric	<input checked="" type="radio"/> 50		
Chronic lymphocytic leukaemia/small lymphocytic lymphoma	1		
Classic Hodgkin lymphoma	1		
Follicular hyperplasia	3		
Kimura disease	2		
Lymphadenitis	6		
Mantle zone hyperplasia	1		
Nodal marginal zone lymphoma	3		
Nodal TFH cell lymphoma, angioimmunoblastic-type	1		
Nodular lymphocyte predominant Hodgkin lymphoma	3		
Paracortical hyperplasia	6		
Polymorphic lymphoproliferative disorders arising in immune deficiency / dysregulation	1		
Progressive transformation of germinal centers	1		
<b>Total</b>	<b>93</b>		

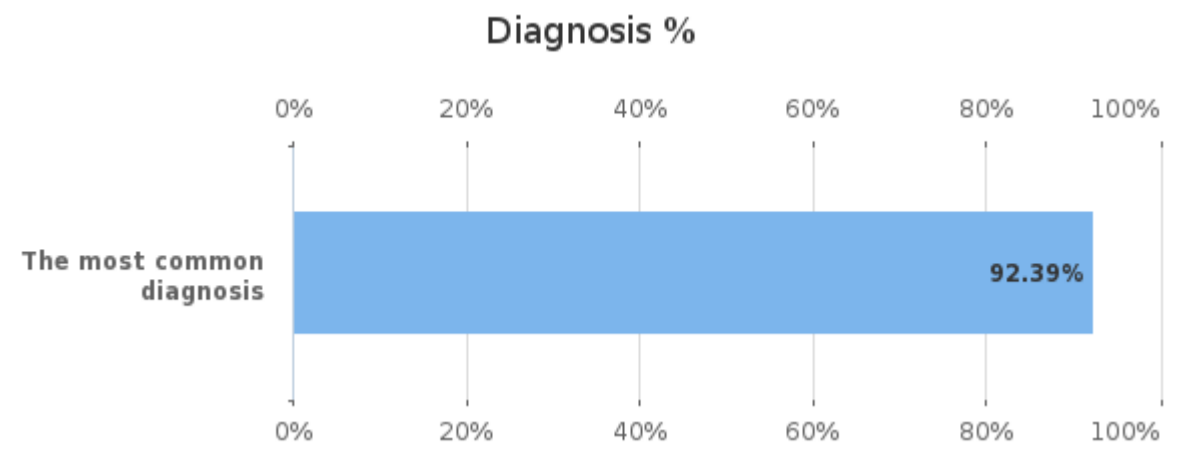
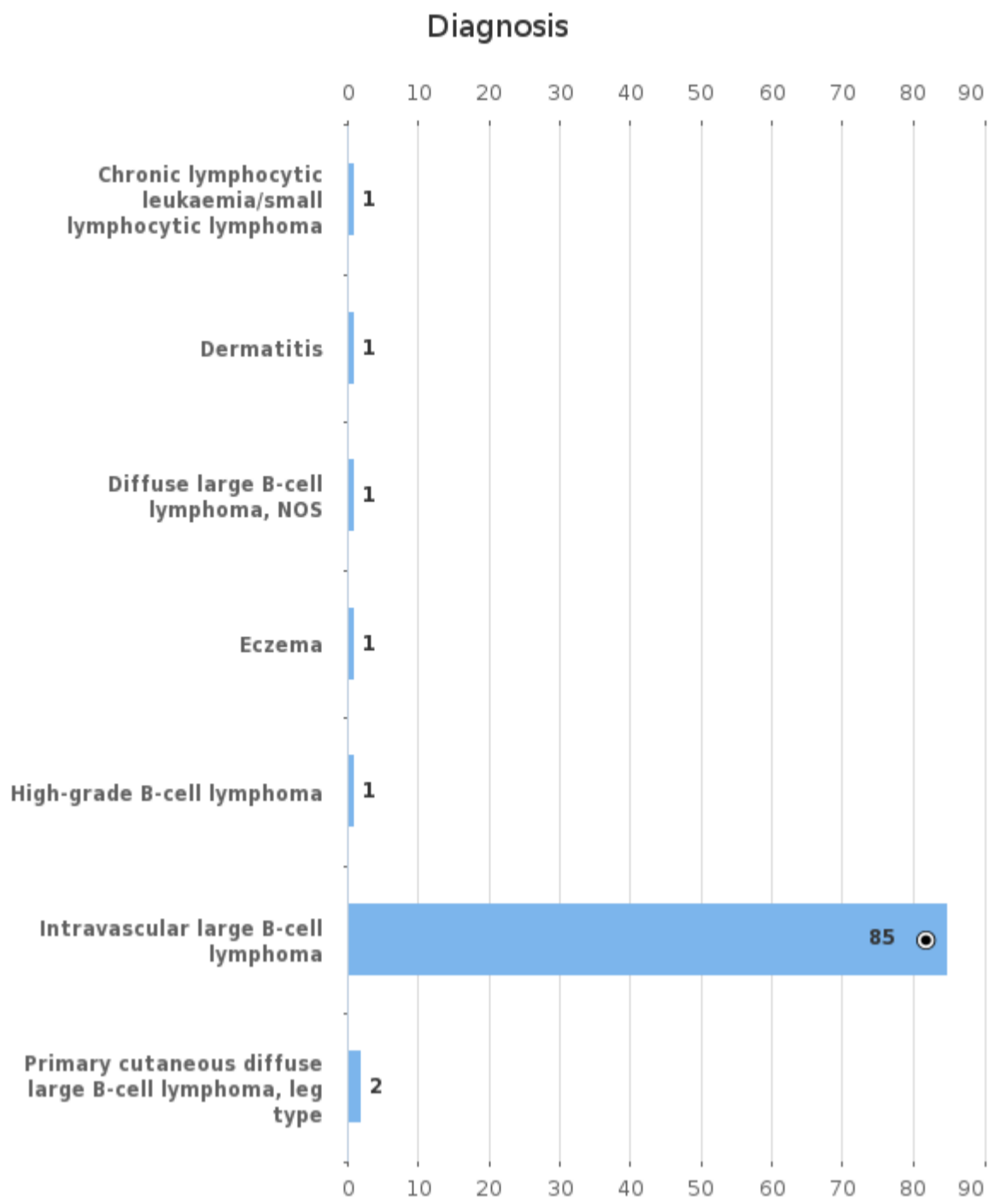
Case 3 | Diagnosis | P.K., E.L.



Diagnosis	n
Chronic lymphocytic leukaemia/small lymphocytic lymphoma	3
Composite lymphoma	17
Follicular lymphoma	2
Mantle cell lymphoma	70
Mantle zone hyperplasia	1
Nodular lymphocyte predominant Hodgkin lymphoma	1
<b>Total</b>	<b>94</b>

Agreement percentage of the responses	%
The most common diagnosis	74.47

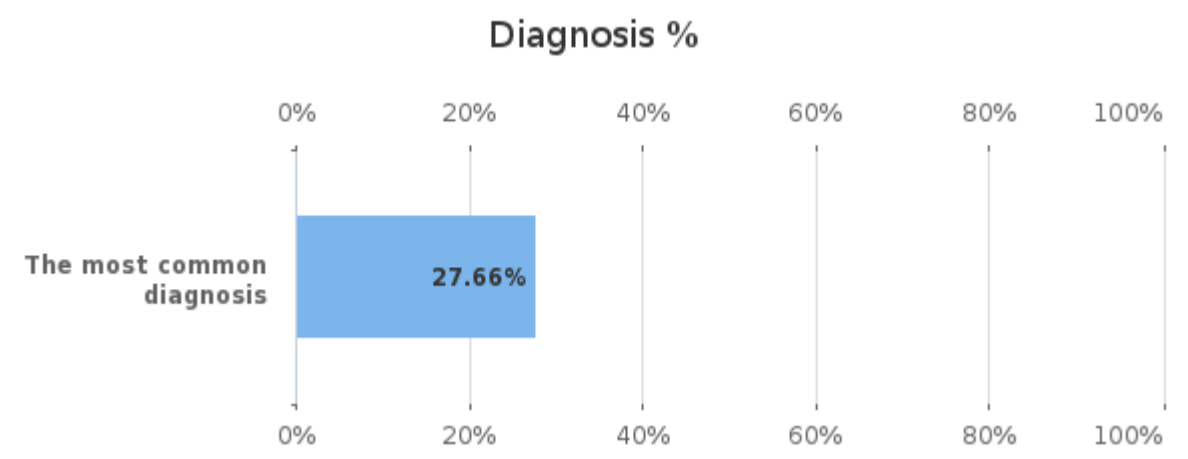
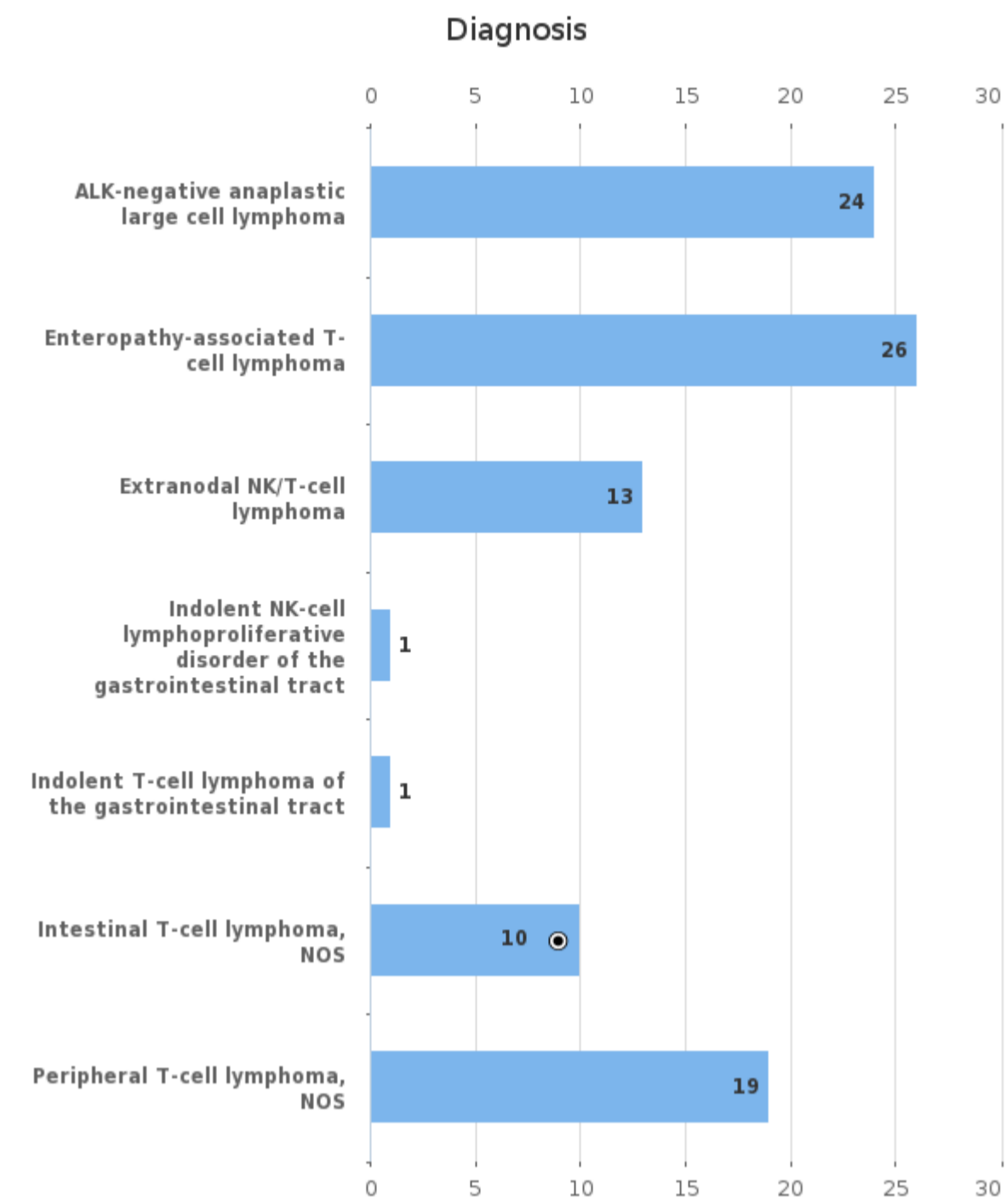
Case 4 | Diagnosis | P.K., E.L.



Diagnosis	n
Chronic lymphocytic leukaemia/small lymphocytic lymphoma	1
Dermatitis	1
Diffuse large B-cell lymphoma, NOS	1
Eczema	1
High-grade B-cell lymphoma	1
Intravascular large B-cell lymphoma	85
Primary cutaneous diffuse large B-cell lymphoma, leg type	2
<b>Total</b>	<b>92</b>

Agreement percentage of the responses	%
The most common diagnosis	92.39

Case 5 | Diagnosis | P.K., E.L.

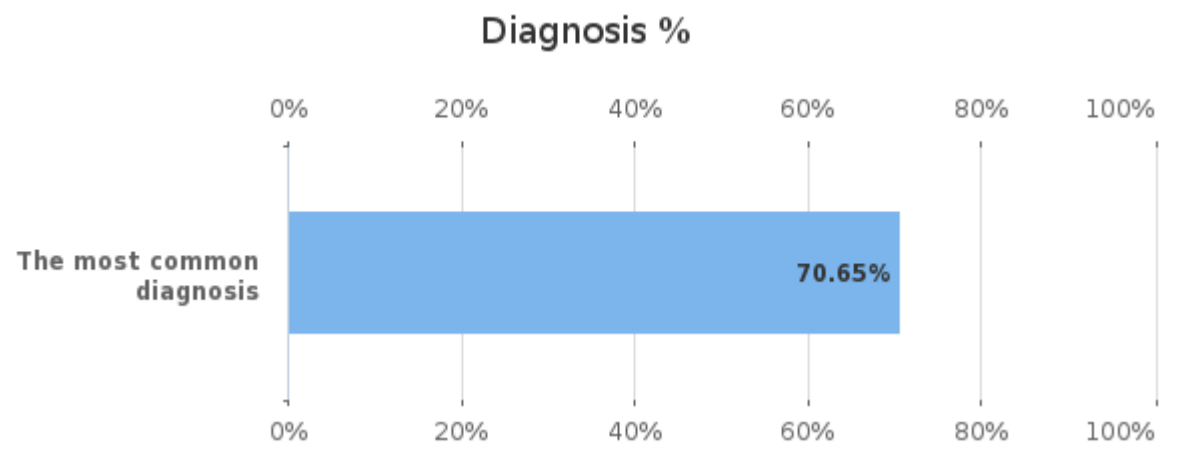
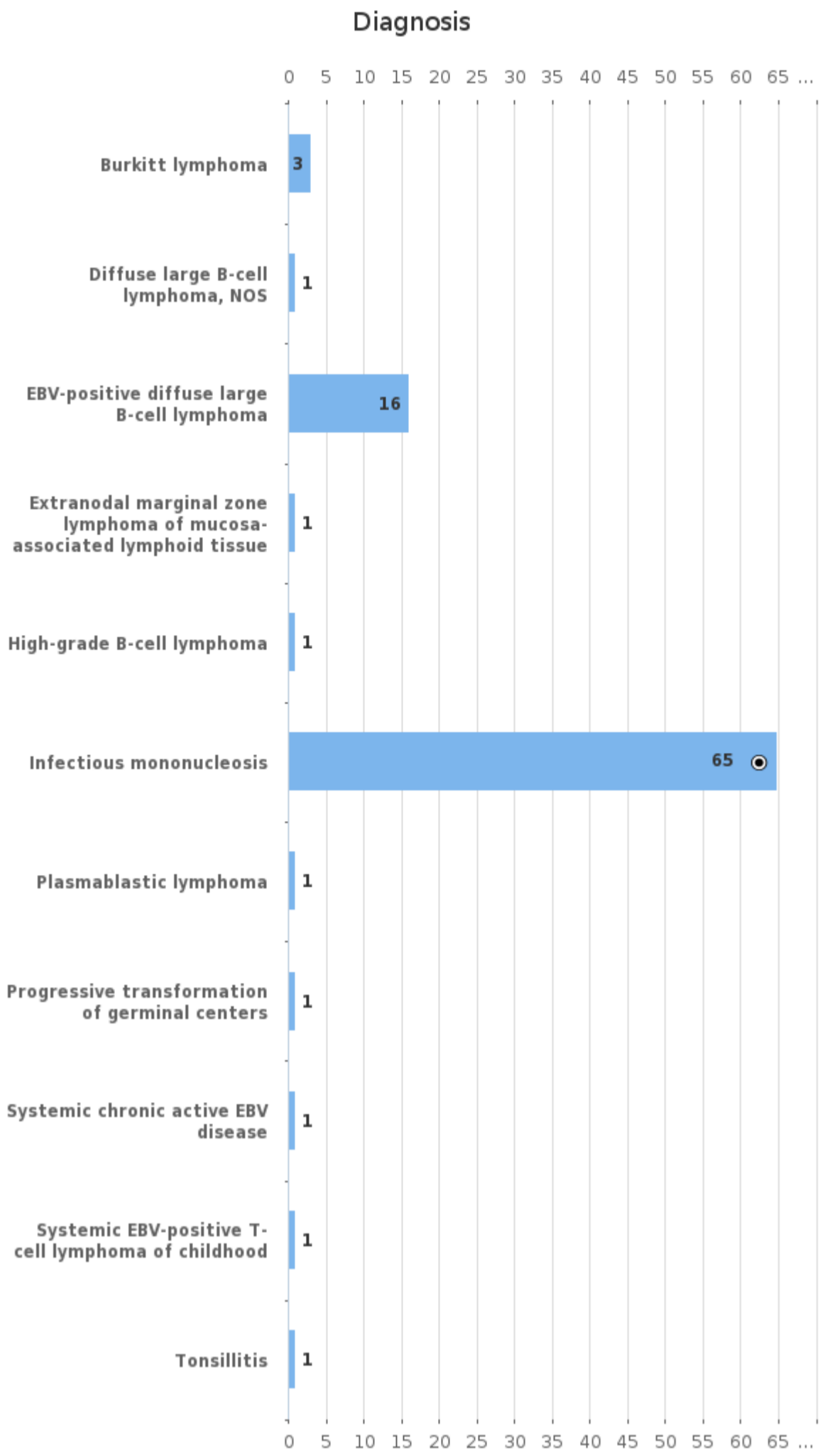


Diagnosis	n
ALK-negative anaplastic large cell lymphoma	24
Enteropathy-associated T-cell lymphoma	26
Extranodal NK/T-cell lymphoma	13
Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract	1
Indolent T-cell lymphoma of the gastrointestinal tract	1
Intestinal T-cell lymphoma, NOS	10
Peripheral T-cell lymphoma, NOS	19
<b>Total</b>	<b>94</b>

Agreement percentage of the responses	%
The most common diagnosis	27.66



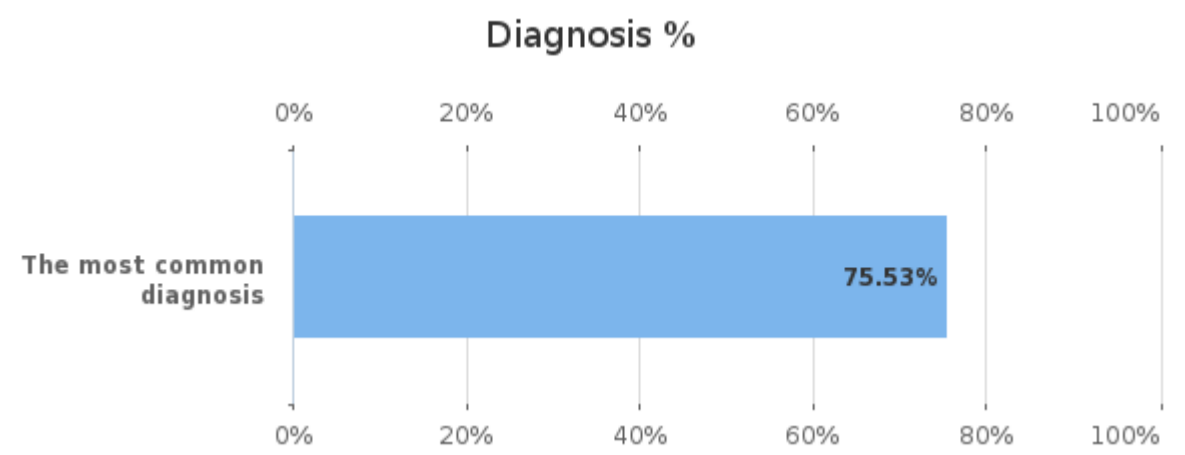
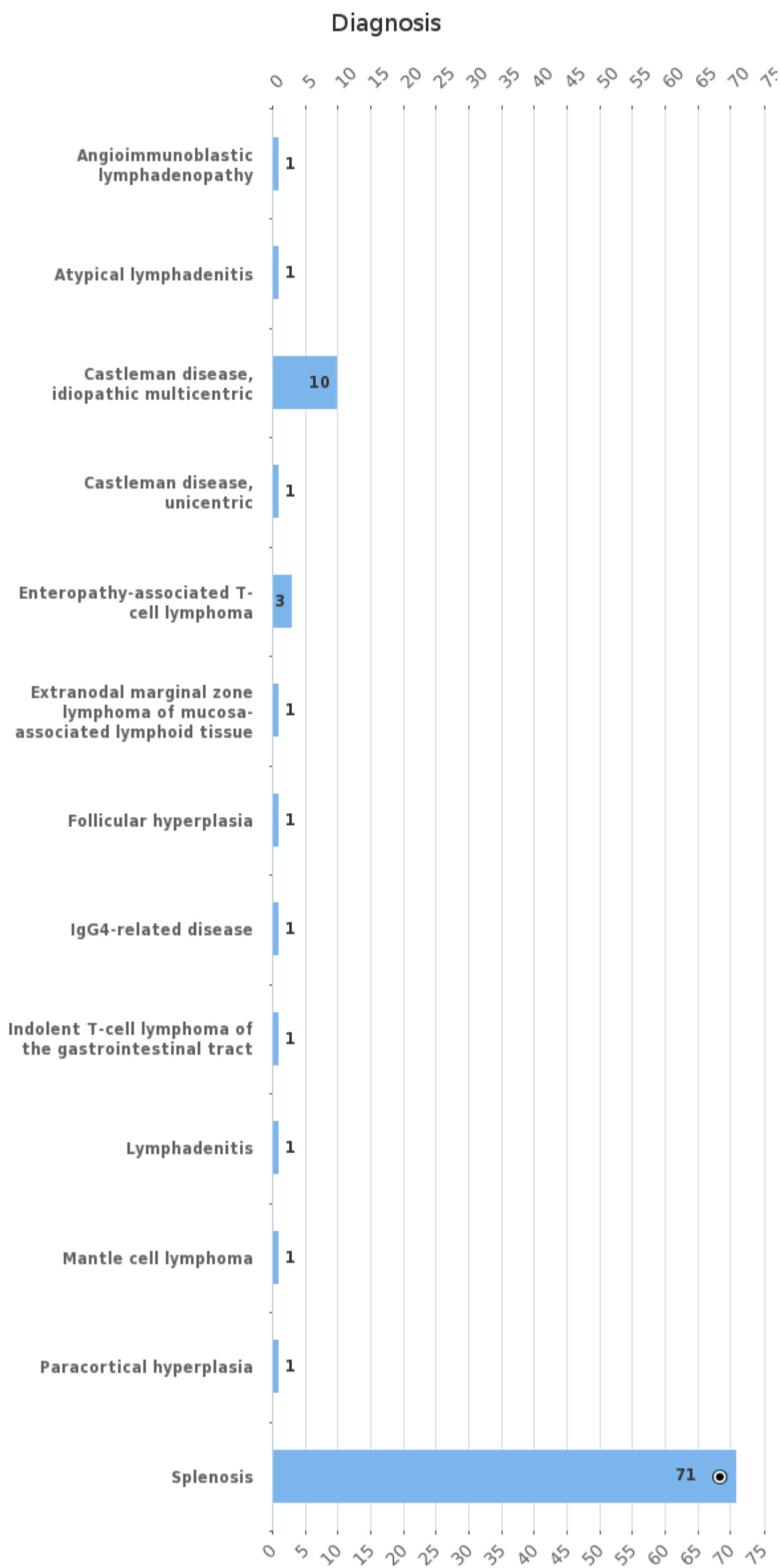
Case 6 | Diagnosis | P.K., E.L.



Diagnosis	n
Burkitt lymphoma	3
Diffuse large B-cell lymphoma, NOS	1
EBV-positive diffuse large B-cell lymphoma	16
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	1
High-grade B-cell lymphoma	1
Infectious mononucleosis	65
Plasmablastic lymphoma	1
Progressive transformation of germinal centers	1
Systemic chronic active EBV disease	1
Systemic EBV-positive T-cell lymphoma of childhood	1
Tonsillitis	1
<b>Total</b>	<b>92</b>

Agreement percentage of the responses	%
The most common diagnosis	70.65

Case 7 | Diagnosis | P.K., E.L.



Diagnosis	n
Angioimmunoblastic lymphadenopathy	1
Atypical lymphadenitis	1
Castleman disease, idiopathic multicentric	10
Castleman disease, unicentric	1
Enteropathy-associated T-cell lymphoma	3
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	1
Follicular hyperplasia	1
IgG4-related disease	1
Indolent T-cell lymphoma of the gastrointestinal tract	1
Lymphadenitis	1
Mantle cell lymphoma	1
Paracortical hyperplasia	1
Splensitis	71

Agreement percentage of the responses	%
The most common diagnosis	75.53

Splenosis	<input checked="" type="radio"/>	71
<b>Total</b>		<b>94</b>

**Report info****Participants**

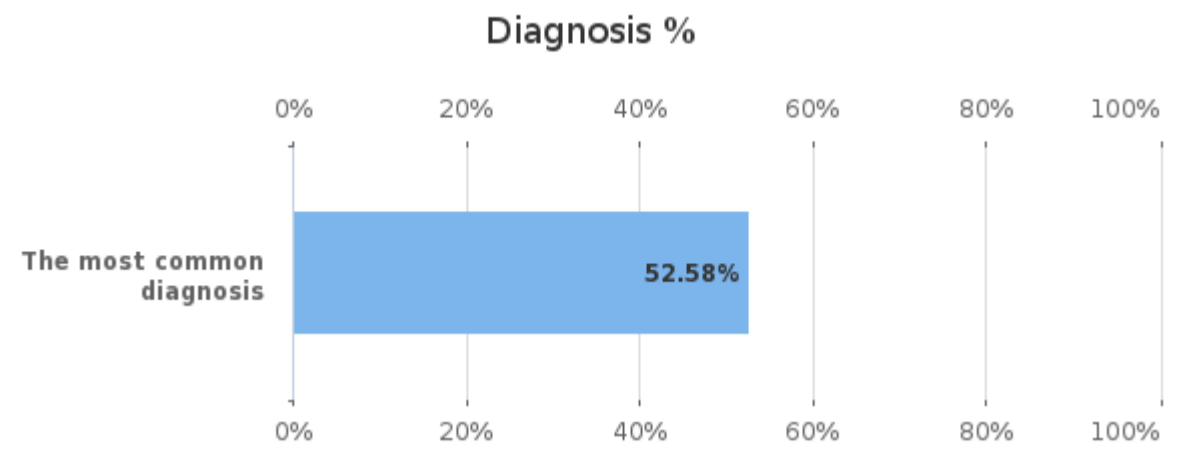
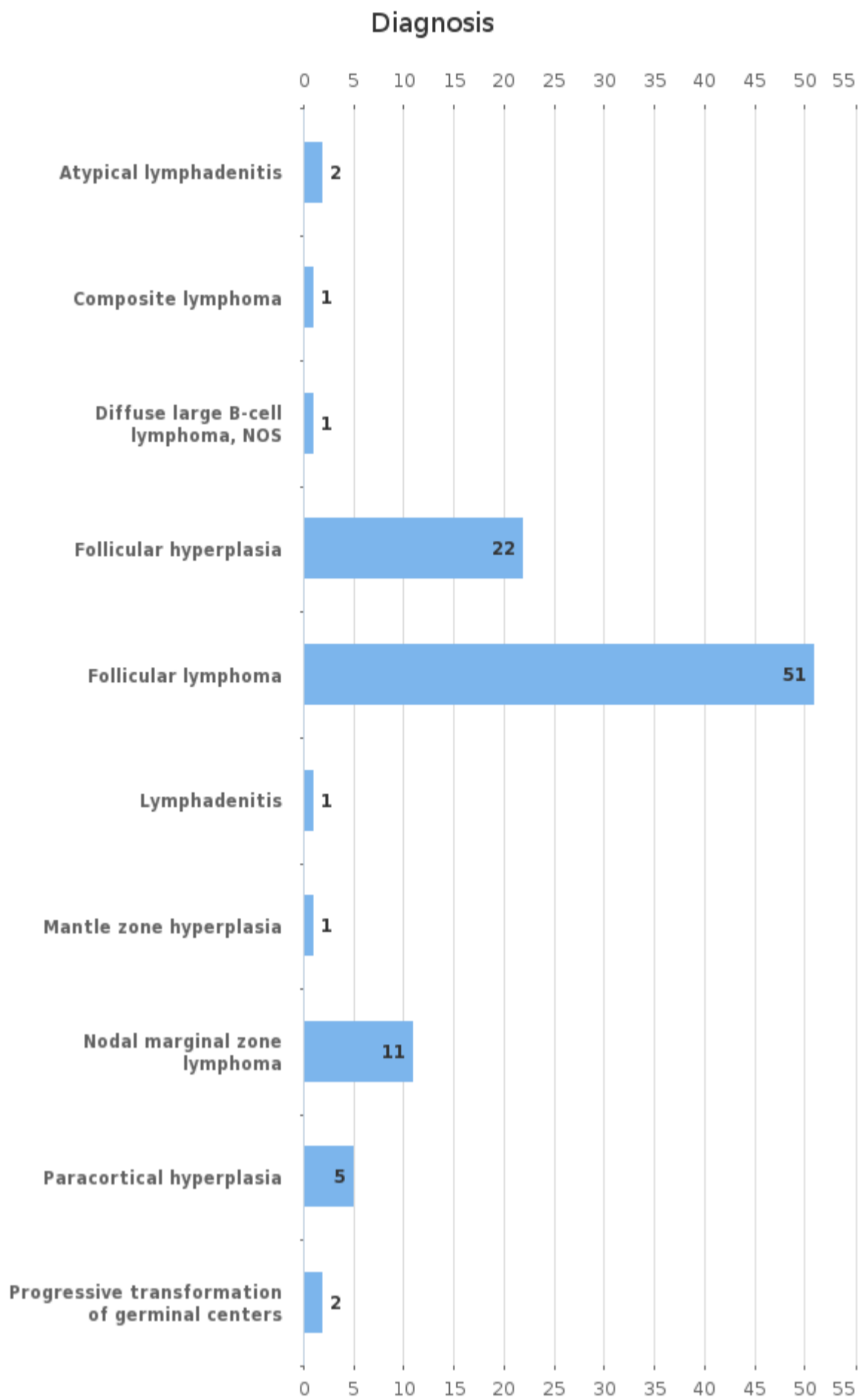
Altogether 96 laboratories from 14 countries participated in this EQA round.

**Report info**

The final report contains distribution of diagnoses and diagnostic agreement. Laboratory's own result is marked with a black radio button . Common instruction guidelines how to interpret the reports can be found under "LabScala user instructions" in LabScala. It is important to take into account that this external quality assessment scheme does not evaluate histopathological examination as a medical consultation. It is intended for interlaboratory comparison including features that may vary between respondents. In case you have any questions regarding the reports, please contact the EQA coordinator.

Round	No of participants	No of responded participants	Response percentage %
Histopathology, virtual microscopy, March, 1-2023	97	85	87.63%

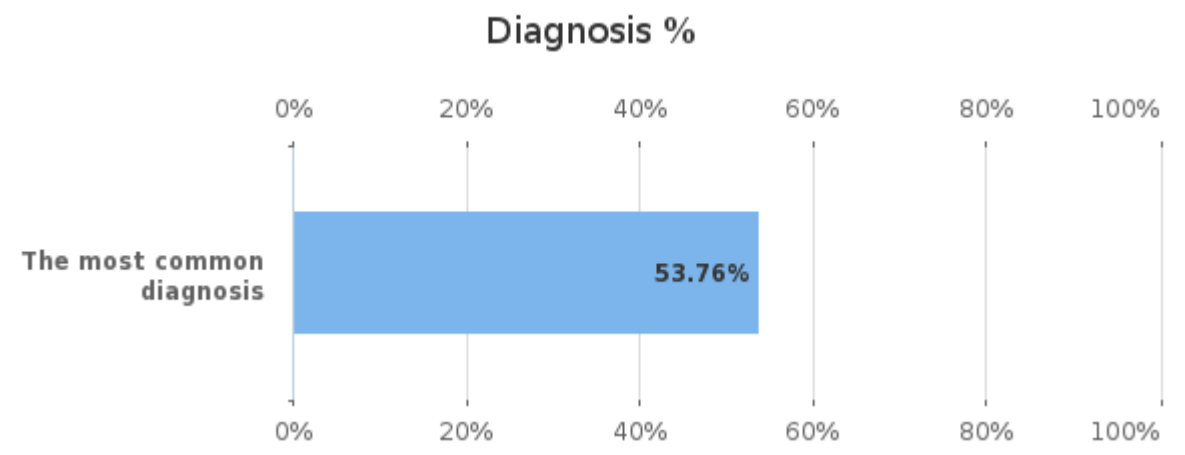
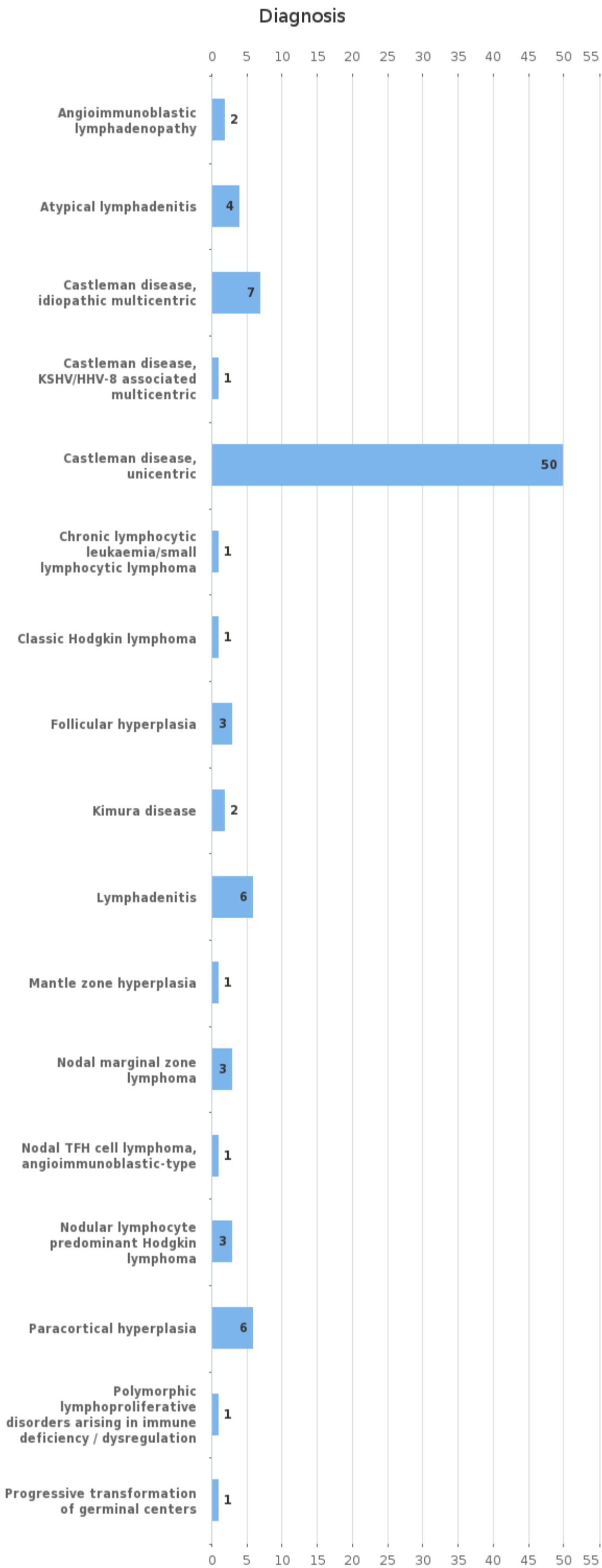
Case 1 | Diagnosis



Diagnosis	n
Atypical lymphadenitis	2
Composite lymphoma	1
Diffuse large B-cell lymphoma, NOS	1
Follicular hyperplasia	22
Follicular lymphoma	51
Lymphadenitis	1
Mantle zone hyperplasia	1
Nodal marginal zone lymphoma	11
Paracortical hyperplasia	5
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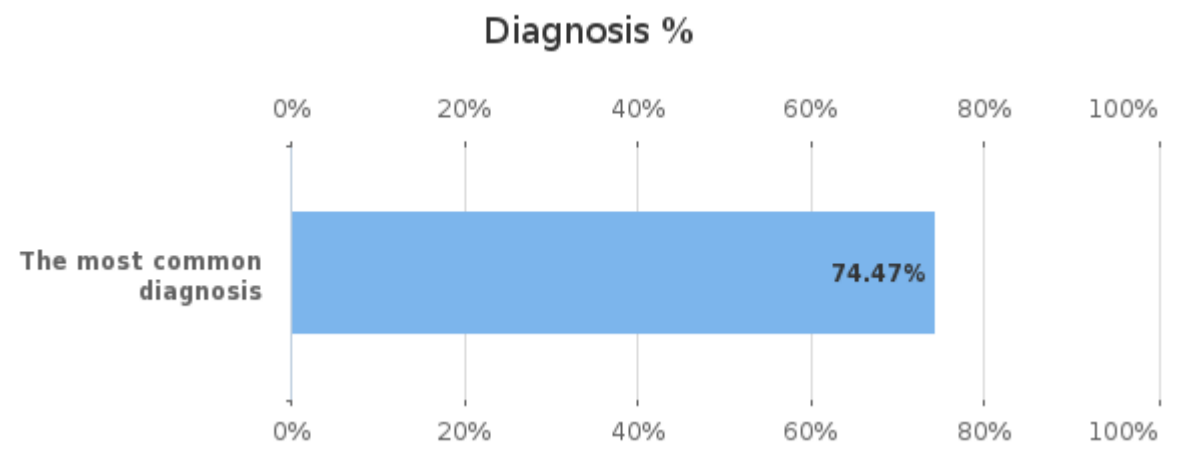
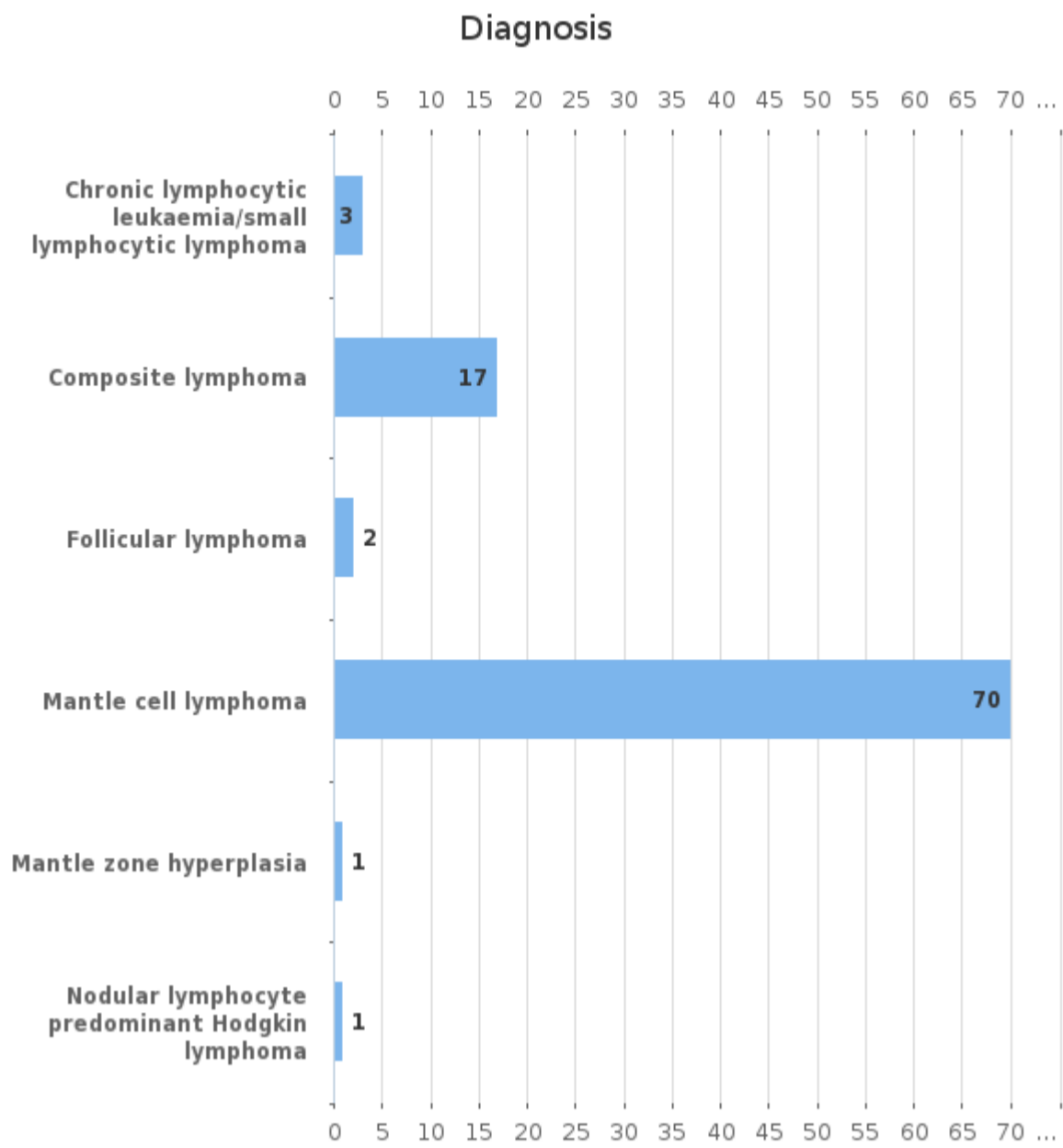
Case 2 | Diagnosis



Diagnosis	n	Agreement percentage of the responses	%
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Angioimmunoblastic lymphadenopathy	2	The most common diagnosis	53.76		
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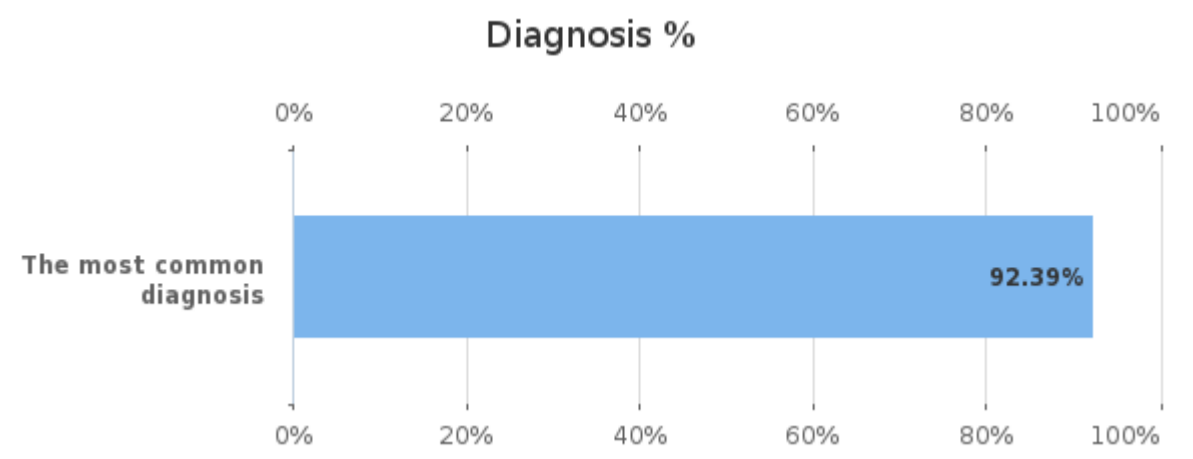
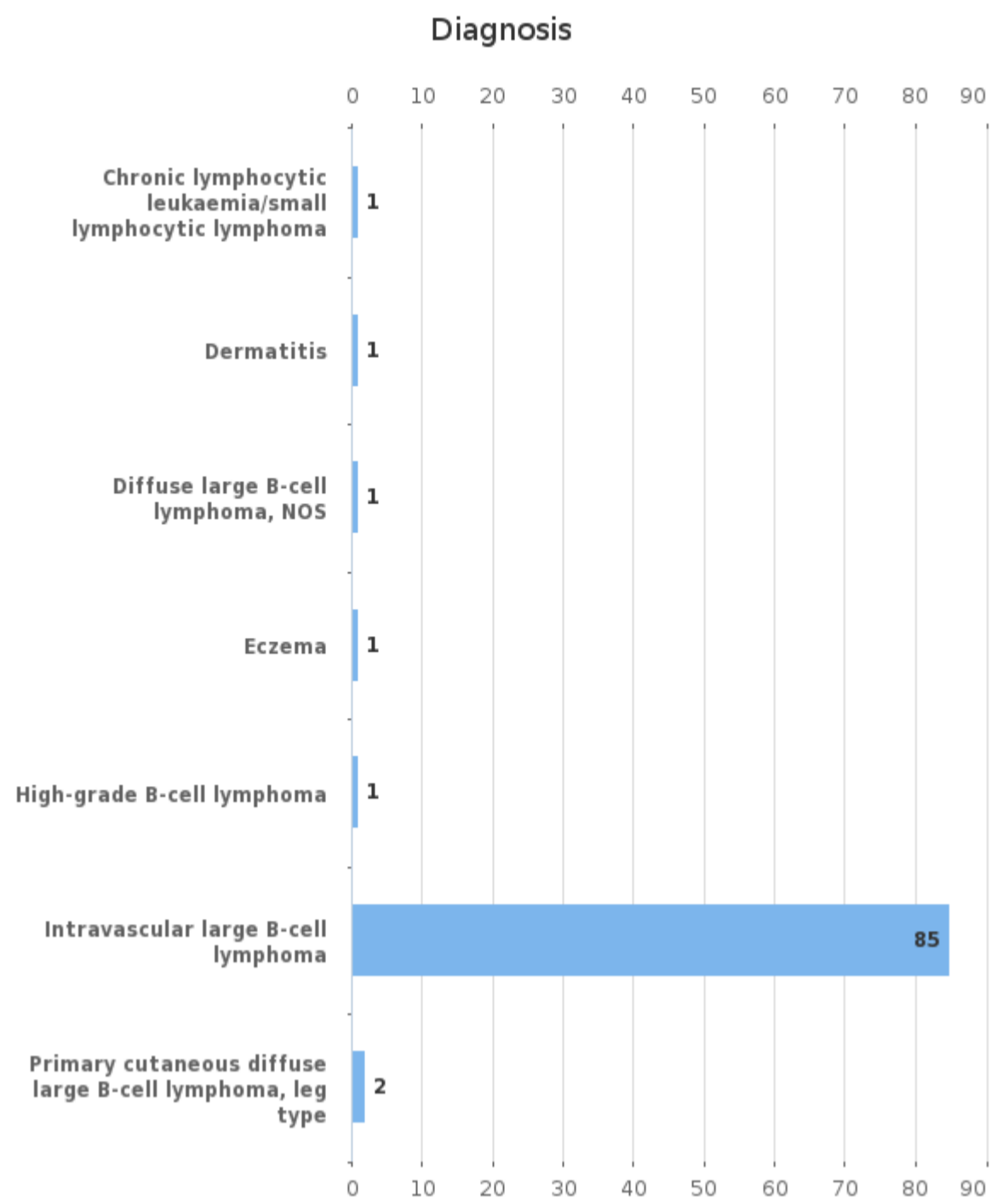


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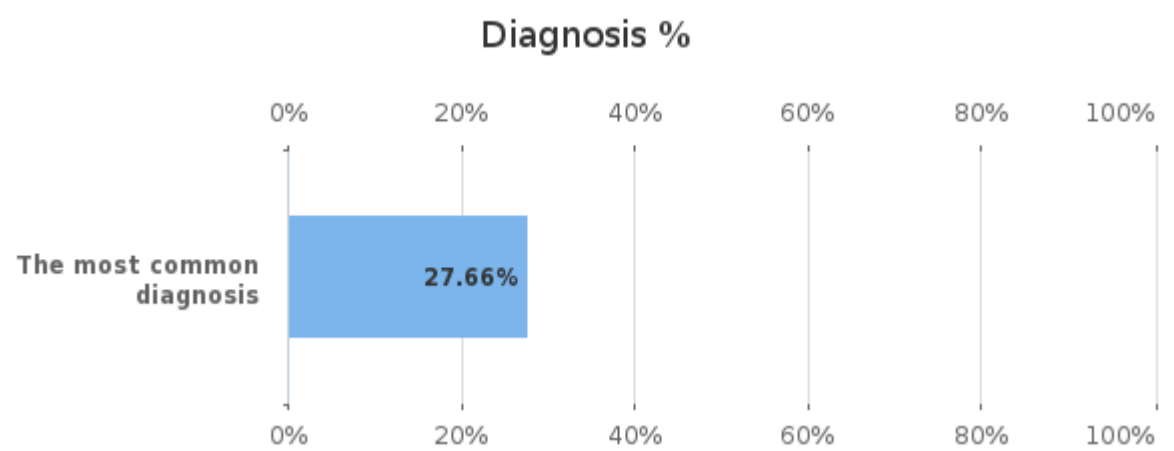
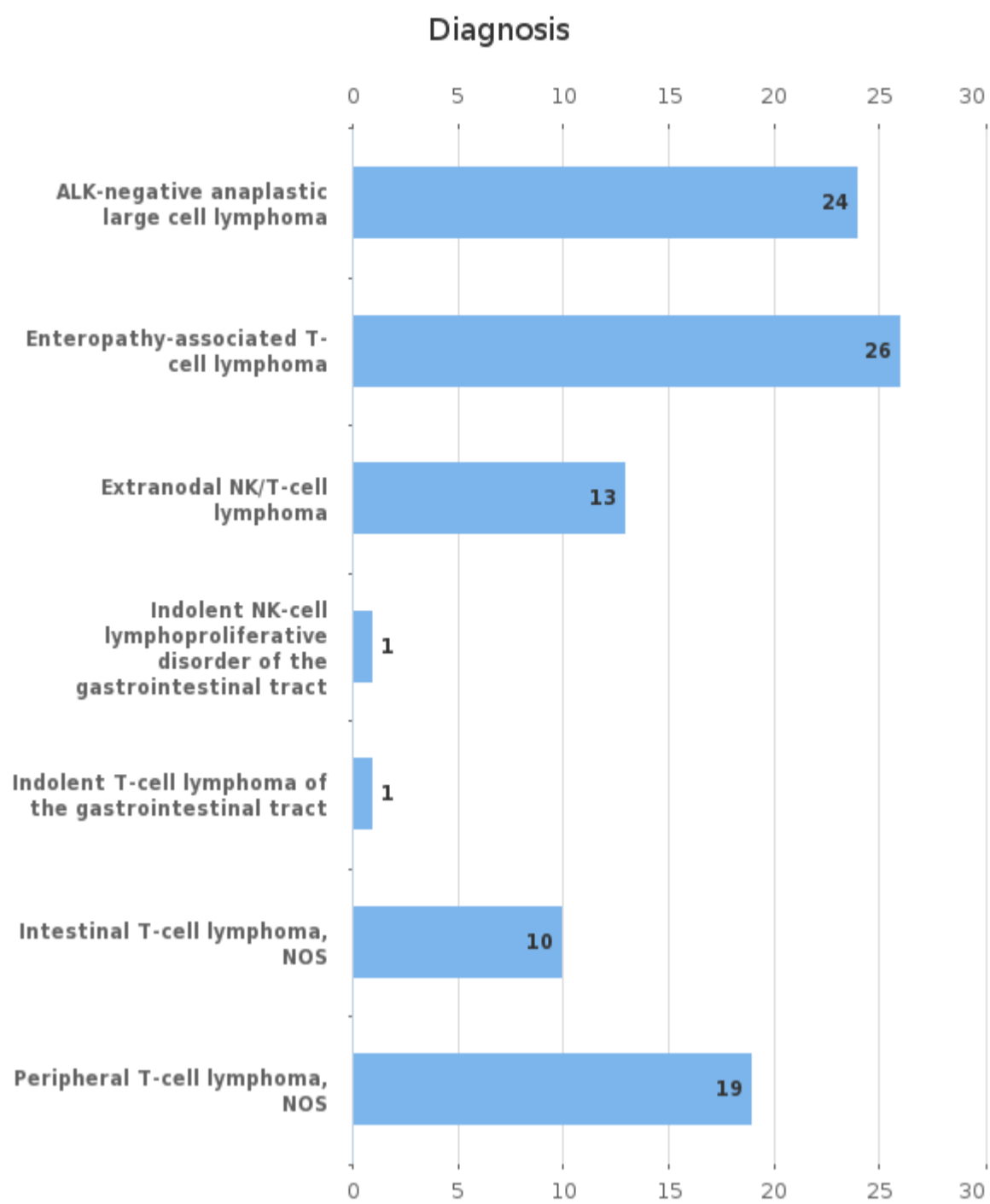
Case 4 | Diagnosis



Diagnosis	n
Chronic lymphocytic leukaemia/small lymphocytic lymphoma	1
Dermatitis	1
Diffuse large B-cell lymphoma, NOS	1
Eczema	1
High-grade B-cell lymphoma	1
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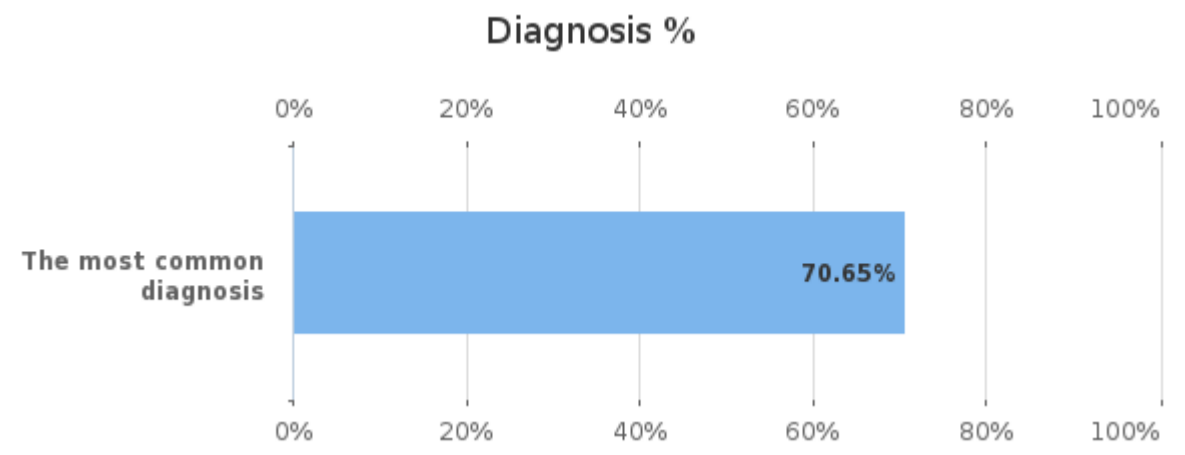
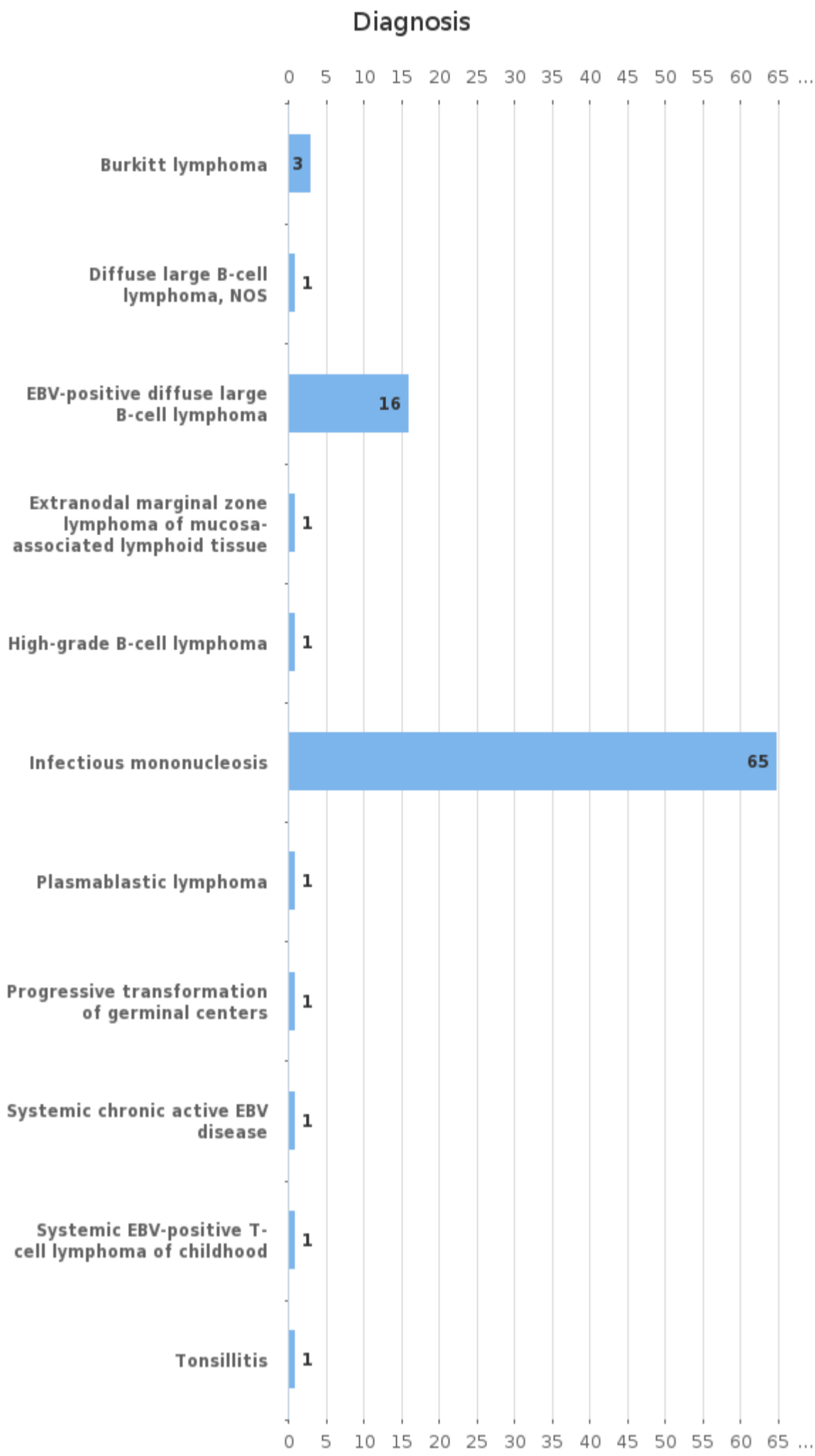
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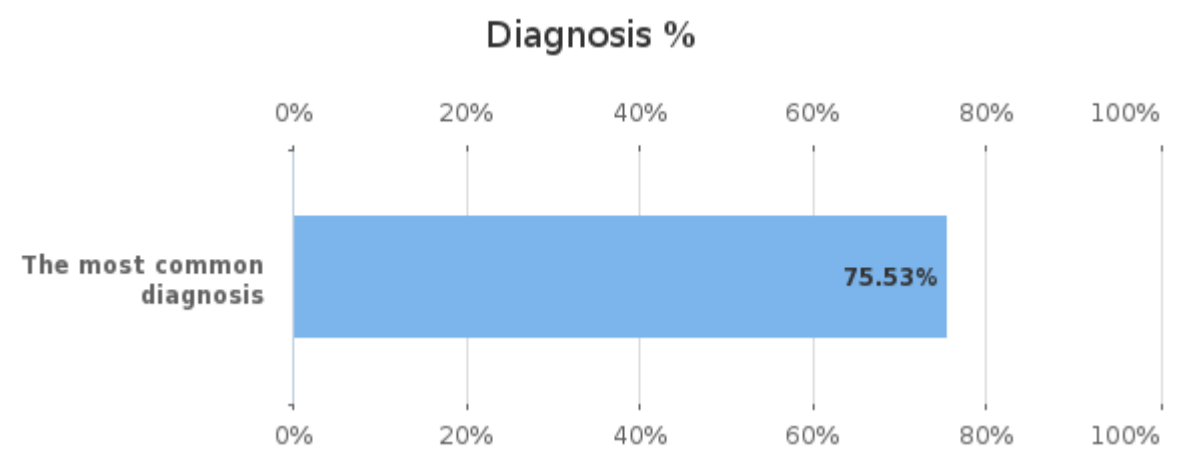
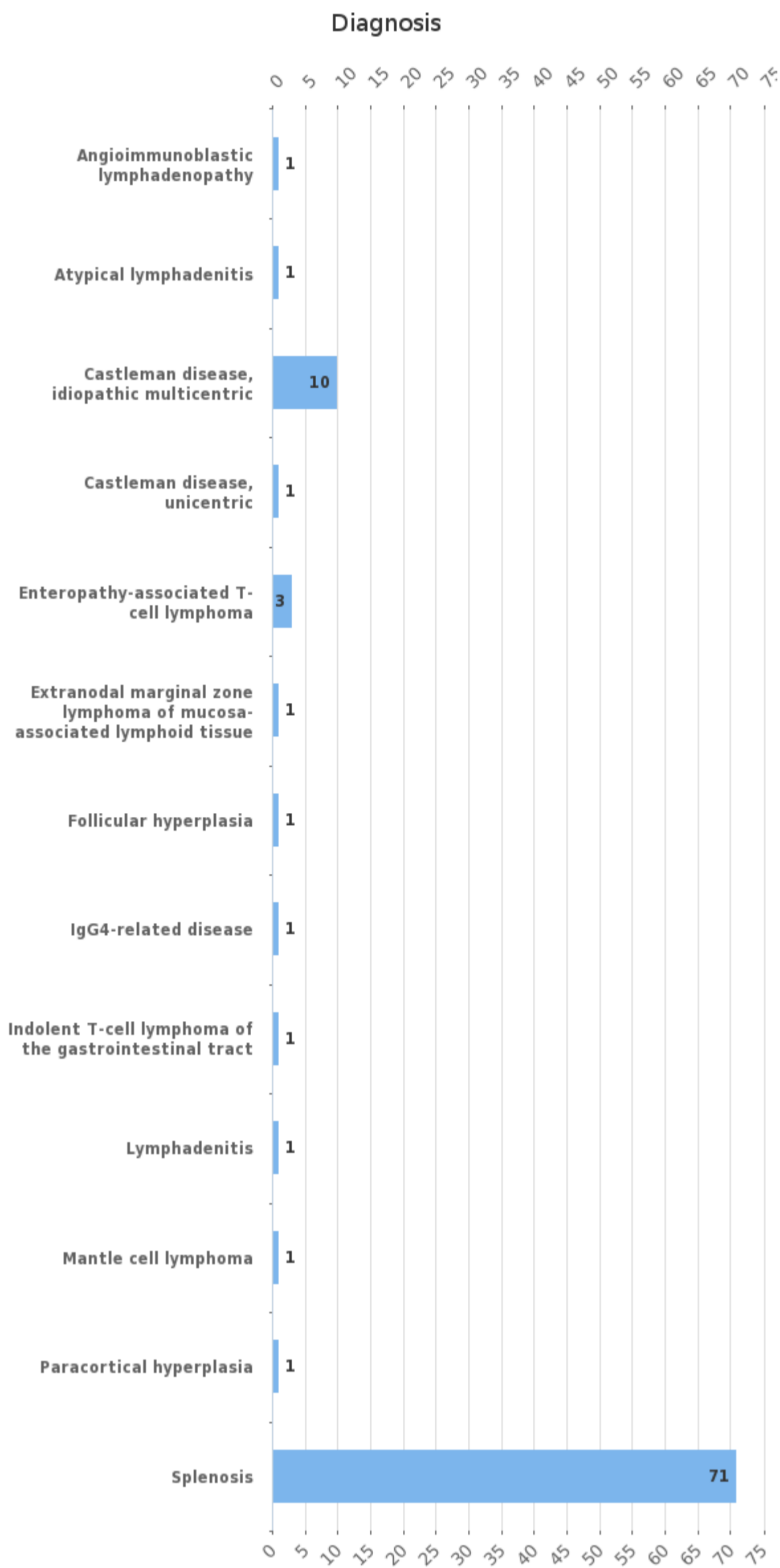
Case 6 | Diagnosis



Diagnosis	n
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EBV-positive diffuse large B-cell lymphoma	16
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Case 7 | Diagnosis



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Enteropathy-associated T-cell lymphoma	3
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Follicular hyperplasia	1
IgG4-related disease	1
Indolent T-cell lymphoma of the gastrointestinal tract	1
Lymphadenitis	1
Mantle cell lymphoma	1
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**Report info****Participants**

Altogether 97 laboratories from 14 countries participated in this EQA round.

**Report info**

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## Histopathology, virtual microscopy: Lymphohematopoietic pathology Round 1, 2023

### Specimens

Sample S001-S007 (LQ778123011- LQ778123017) were virtual microscopy images. Topic of this round was Lymphohematopoietic pathology. There were seven cases of which patient's available data of clinical history were given. The samples had been fixed with formalin. The participants were asked to give an interpretation comparable to normal clinical situation, i.e. the diagnosis. The samples of this round were given only as virtual images.

### Report info

Please see the description of the data analysis on the last page of the laboratory-specific histograms and Numerical Summary reports.

### Comments – Expert

The round's diagnoses are based on WHO (WHO classification of Haematolymphoid Tumours 2016 revised 4th edition or 2022 5th edition beta version) and ICC (The International Consensus Classification of Mature Lymphoid Neoplasms: a report from the Clinical Advisory Committee. Blood. 2022 Sep 15; 140(11): 1229-1253) classifications.

A few comments were received about the quality of the photos of the round. Originally, all slides were to be scanned. However, this was not possible, so as a compromise we ended up scanning only HE, CD20, CD3 and CD5 stainings and taking pictures of the other stainings in a representative area. We apologize for that, the solution certainly made it difficult to interpret the samples.

### Case 1 (S001: LQ778123011)

A 77-year-old man. Laparoscopic lymph node biopsy for suspected lymphoma.

Diagnosis: Follicular lymphoma, grade 1-2 (WHO 2016, ICC)  
Classic Follicular lymphoma (WHO 2022)

A follicular structure can be seen throughout the sample, but the follicles are poorly defined with no polarization or macrophages. The histological view is therefore strongly suspicious of follicular lymphoma. Immunohistochemically, however, the follicular cells remain bcl-2 negative. However, flow cytometry showed that the CD10-positive B cells were lambda clonal, and chromosome analysis showed IGH-BCL2 translocation t(14;18)(q32;q21).

In the differential diagnosis with follicular hyperplasia, it should be taken into account that some follicular lymphomas are immunohistochemically bcl-2 negative, and bcl-2 translocation cannot always be detected either. In these cases, immunoglobulin heavy or light chain rearrangement studies have their place in diagnostics. As many respondents suggested, in such a cases it would be worthwhile to confirm the immunohistochemical negativity with yet another antibody clone.

### Case 2 (S002: LQ778123012)

A 69-year-old woman. 2012 left breast cancer, resection, axillary evacuation, chemotherapy, hormonal therapy and radiotherapy. Enlarged lymph nodes on the left side of the neck in the control ultrasound, the largest being 33 x 13 mm in size. A lymph node sample from the neck.

Diagnosis: Catleman's disease, Unicentric ("Hyaline vascular type")

2023-06-05

### FINAL REPORT

Product no. 6542

Subcontracting: Sample preparation,  
Digital image services

Samples sent	2023-03-28
Round closed	2023-05-02
Final report	2023-06-05

### Request for correction

Typing errors in laboratory's result forms are on laboratory's responsibility. Labquality accepts responsibility only for result processing. Requests must be notified by writing within three weeks from the date of this letter.

### Authorized by

EQA Coordinator

Pia Eloranta

pia.eloranta@labquality.fi

### Expert

Samuli Vaittinen

Ph.D., Specialist in pathology

TYKS Laboratoriotuomioalue, Patologia

### Labquality Oy

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In the lymph node, you can see a lot of regressed, onion skin-like follicles, of which the follicular cells have mostly disappeared and you can actually see only dendritic cells. Hyperplasia of the mantle cell zone is also typical, as is a common mantle zone surrounding several follicles (not seen in this sample). In places, you can see a hyaline blood vessel protruding into the follicle, forming a lollipop structure. In addition, paracortical hyperplasia and vascular proliferation appear. Often in this variant, fibrosis of the lymph node capsule and/or fibrotic septa are also seen, which are not visible in this sample. No significant plasma cell excess is seen.

In the differential diagnosis one must exclude low grade lymphomas, mantle zone hyperplasia and in situ mantle cell neoplasia. In this case, immunohistochemistry had been done quite sparingly, but flow cytometrically, the B cells were polyclonal. The lymph node was surgically removed and the patient is doing well without other treatments after 4 years of follow-up.

### **Case 3 (S003: LQ778123013)**

A 77-year-old man. Hospitalized due to shortness of breath, pleural fluid. Large number of prominent lymph nodes on both sides in the armpits, neck, clavicles and groin in the CT examination. Large spleen, ad 21cm, with non-specific lesion in the lateral part. A lymph node sample.

Diagnosis: Composite lymphoma (Follicular lymphoma, grade 1-2 and Mantle cell lymphoma)

This is a composite lymphoma, in which two different lymphomas are seen in the lymph node at the same time. The first one represents mantle cell lymphoma, in which diffusely growing cells are CD20+, CD5+, CD43+ and Cyclin-D1+. The mitotic activity is quite high in places, the cells are medium sized, the chromatin is fine and several inconspicuous nucleoli are seen. Based on this, the lymphoma could already be considered as a blastoid variant. The second component is follicular lymphoma, where the cells are CD20+, CD10+, bcl-6+ and bcl-2+.

Similar cell clones were also found by flow cytometry, and the chromosome studies showed IGH-BCL2 translocation t(14;18)(q32;q21) in some cells and CCND1-IGH translocation t(11;14)(q13;q32) in others. Composite lymphomas are not as rare as one might assume and may go unnoticed, if the sections are not carefully examined thoroughly after one has already diagnosed one lymphoma.

### **Case 4 (S004: LQ778123014)**

86-year-old man, hypertension, MCC, 2010 myocardial infarction, when PCI + stenting. Symptoms of infection for 2 weeks, despite antibiotic treatment, inflammation values persisted high, focus of infection unclear, liver chemistry elevated. On the upper body a vague, purplish skin change with slight ring-like formations, no ulcers, no itching. Vasculitis, exanthema consistent with borrelia, infection/drug?

Diagnosis: Intravascular large B-cell lymphoma

Most of the respondents identified the disease correctly (even if the quality of the immunostainings was not the best possible). The skin sample shows intravascular atypical B cells with the immunophenotype CD20+, MUM-1+, CD5+, CD10-/(+), BCL-2+, BCL-6(+), ALK1-, CD30-, CD34- and TdT- .

Intravascular large B-cell lymphoma can occur in almost any organ and the symptoms depend on the localization of the disease. Often however, patients have general symptoms. A "cutaneous subtype" is limited to the skin and patients often do not have general symptoms. The clinical skin manifestation can look very diverse. The lymphoma cells proliferate virtually exclusively within the lumens of the vessels, which distinguishes the disease from e.g. primary skin diffuse "leg type" large B-cell lymphoma.

### **Case 5 (S005: LQ778123015)**

A 76-year-old woman. Weight loss, loss of appetite. A carcinoma-like area in the ventricle on the small curvature, hard for biopsy forceps. Sample 1 normal duodenum, sample 2 normal antrum and samples 3 from the suspected carcinoma.

Diagnosis: Enteropathy-associated T-cell lymphoma

Atypical T cells with an immunophenotype of ALK1-, CD3+, CD5-, CD7+, CD4 mainly – (macrophages and non-specific staining is seen), CD8-, CD56- , CD30 partly + (varying in intensity), CISH/EBER-, TIA1 partly + and granzyme B partly + are seen in the corpus. The disease is strongly associated with celiac disease. The most common localization is the jejunum, but the disease is also seen elsewhere in the small intestine, large intestine and stomach. Patients are often symptomatic (malabsorption, weight loss, abdominal pain, perforation).

In the duodenum, the villi are slightly clumsy. Intraepithelial lymphocytes (IEL) are increased in both the duodenum and the antrum, but their immunophenotype is different from each other. In the duodenum, these are CD3+, CD5+ and CD8+, corresponding to normal, so at least refractory celiac disease type 2 does not come into question. In the antrum, these are abnormally CD3+, CD5- and CD8-, corresponding to tumor cells and referring to neoplastic cells.



In terms of differential diagnosis, ALK-negative anaplastic large T-cell lymphoma could come into question, but in that case the lymphoma cells should be strongly CD30 positive throughoutly. Extranodal NK/T cell lymphoma should preferably be CD56 positive and at least EBV positive. The patient's disease was treated to remission with CHOP and MINE cytostats and complementary radiotherapy. However, the disease relapsed already after 6 months, also spread to the lungs and liver, and the patient died.

**Case 6 (S006: LQ778123016)**

A generally healthy 16 years old boy. A sore throat and enlarged lymph nodes. The tonsils fill the entire oropharynx, emergency tonsillectomy performed.

Diagnosis: Infectious mononucleosis

The patient's age and medical history are strongly suggestive for mononucleosis and mononucleosis quick test was positive. The diagnosis of malignant lymphoma should be considered very carefully with this history. The EBV-positive reactive immunoblast reaction may be very atypical and sheet-like. Reed-Sternberg type cells can also often be seen. An aberrant immunophenotype can be seen, as in this case CD20 and CD43 were both positive. In mononucleosis, however, this is not necessarily a malignant feature. A diagnosis of mononucleosis is supported by abundant EBV positivity in both small and larger lymphocytes, mainly preserved general structure (follicular structures are seen) and polymorphic B-cells with plasmacytoid differentiation.

In this case, the patient recovered quickly, which confirmed the benign diagnosis. Clonality studies could be useful, but weak clonal or oligoclonal products are often found in mononucleosis, the interpretation of which may be problematic.

**Case 7 (S007: LQ778123017)**

A 43-year-old man. A tumor on the surface of the ileum, approximately 2 x 4 cm in size, was found to be the cause of intestinal bleeding. Only a small ulceration on the mucosa. Dozens of similar smaller tumors are seen all over the surface of the small intestine, in the mesentery and peritoneum. A sample taken from the surface of the proximal small intestine.

Diagnosis: Splenosis

Histologically, the sample shows normal spleen tissue, which could represent either an accessory spleen or a splenosis. Splenosis is a benign acquired condition characterized by the presence of heterotopic viable splenic tissue in other organs or within cavities such as peritoneum, retroperitoneum, or thorax after splenic trauma or surgery. Multiple lesions are often seen. This patient had his spleen removed in childhood in connection with an abdominal injury.

**End of report**

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