Hull University Teaching Hospitals NHS Trust

Hull University Teaching Hospitals and North Lincolnshire NHS Trusts Haematology Multidisciplinary Team Guideline and Pathway

Hodgkin Lymphoma

1 BACKGROUND

The Hull and North Lincolnshire Haematology Multidisciplinary team manages patients with haematological malignancies on three sites, Diana Princess of Wales Hospital Grimsby, the Queens Centre for Haematology and Oncology at Castle Hill Hospital Hull University Teaching Hospitals NHS Trust and Scunthorpe Hospital.

Levels of service provided in these organisations is as defined in the NICE guidance "Haematological Cancers: improving outcomes NG47" 25th May 2016.

Low-to-intermediate intensity chemotherapy is delivered in Grimsby, the Queens Centre Castle Hill Hospital and Scunthorpe Hospital.

High-intensity chemotherapy and autologous stem cell transplantation is delivered at the Queens Centre, Castle Hill Hospital.

The following chemotherapy regimens for Hodgkin Lymphoma (HL) can be delivered in centres providing low-to intermediate intensity chemotherapy:

ChlVPP

Vinblastine single agent

Rituximab single agent

The following chemotherapy regimens for HL can only be delivered in centres providing high intensity chemotherapy:

Escalated BEACOPP

ABVD/AVD

RCVP

RCHOP

DHAP

IVE

ICE

BEAM autoPBSC

LEAM autoPBSC

Brentuximab

Nivolumab

Pembrolizumab

2 POLICY / PROCEDURE / GUIDELINE DETAILS

Diagnosis of Hodgkin Lymphoma.

HL will be diagnosed in line with current BSH guidelines: First line management of classical Hodgkin Lymphoma, published 09/04/2014 and Investigation and management of Nodular Lymphocyte Predominant Hodgkin Lymphoma, published 05/11/2015.

Patient's referral with a suspected lymphoproliferative disorder are to be reviewed by a haematologist who decides about timescale of the first appointment - to be offered in accordance with relevant NHS patient pathway. Booking instructions for the first clinic appointment should include a panel of routine blood tests: full blood count, group and screen, DAT, biochemical profile, lactate dehydrogenase, B2 microglobulin, serum protein electrophoresis, coagulation screen, virology screen (hepatitis B - S antigen, hepatitis C antibody, HIV, varicella zoster antibody). Additional blood tests are to be requested at clinician discretion - relevant to the referral details.

Diagnostic material (lymph node or soft tissue biopsies, bone marrow) is to be sent directly to HMDS, Leeds. Lymph node excision biopsy is strongly recommended, but if risk of a surgical procedure outweighs the potential benefits of an excision biopsy – multiple needle core biopsies is an alternative.

Based on HMDS report - diagnosis is to be defined as Classical Hodgkin Lymphoma (cHL) with specified subtype or Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL).

Full body PET/CT scan is an obligatory staging scan modality.

Early stage cHL (Ann Arbor IA and IIA) patients may be classified as favorable or unfavorable based on EORTC criteria.

Risk stratification and prognostication for advanced stage cHL (Ann Arbor III and IV) is to be assessed in accordance with International Prognostic Score (Hasenclever Index)

There is currently no evidence to support a risk-stratified approach to therapy in early stage Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL) and there is no internationally validated scoring system for advanced stage NLPHL.

Staging bone marrow biopsy is not routinely required but may be recommended if clinically appropriate (i.e. ambiguous bone marrow involvement on PET/CT scan or unexplained cytopenias).

All patients with reproductive potential requiring anti-cancer treatment should be fully informed prior to treatment about the possible gonadal toxic consequences of any given treatment approach. Fertility-preserving treatments should be offered to eligible patients in accordance with guidelines: "The effects of cancer treatment on reproductive functions:" RCP 2007

All newly diagnosed cases of HL are to be discussed at the network MDT.

Management of Hodgkin Lymphoma

cHL will be managed within the Hull and North Lincolnshire MDT in line with current BSH guidelines: First line management of classical Hodgkin Lymphoma, published 09/04/2014, Investigation and management of Nodular Lymphocyte Predominant Hodgkin Lymphoma, published 05/11/2015 and Guideline on the management of primary resistant and relapsed classical Hodgkin lymphoma, published 01/10/2013.

The local management of HL will also take account of the following NICE pathways and guidance:

Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma
NICE guidance TA462, published 26/07/2017

Pembrolizumab for treating relapsed or refractory ... - NICE
NICE guidance TA540, published 3/9/2018

Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma
NICE guidance TA446, published 28/06/2017

First line-treatment of Hodgkin Lymphoma.

Classical Hodgkin Lymphoma

Treatment decisions are to be based on a risk stratified approach for cHL. Treatment decisions concerning elderly patients are to be based on assessment of fitness/frailty and co-morbidities rather than age alone.

Early stage cHL patients IA and IIA without bulk are to be offered ABVD based treatment (doxorubicin, bleomycin, vinblastine, dacarbazine) with interim PET/CT scan assessment. Recent studies indicate that risk stratification of early cHL is less predictive than PET response and therefore we will not routinely use it to guide treatment. In light of the results of the RAPID and other similar trials each patient needs to be assessed and counselled in relation to the risks and benefits of radiotherapy in the treatment of their disease. Standard therapy would be with 2 cycles of ABVD and radiotherapy (RT) with PET assessment pre-treatment and post therapy. If the patient and MDT feel it would be appropriate to try to avoid radiotherapy and accept the small increase in relapse then treatment should proceed as per the RAPID protocol with PET pre-treatment and after 3 ABVD. If the PET is negative (Deauville 2) then no further treatment is required. If the PET is positive then a further cycle of ABVD is given followed by radiotherapy and an end of treatment PET.

Patients with advanced stage cHL fit for intensive chemotherapy should initiate treatment with 2 cycles of ABVD chemotherapy and then undergo risk stratification based on interim PET/CT scan result:-

- Patients with complete response (Deauville 2) on interim PET/CT are to continue ABVD chemotherapy up to planned 6 cycles with no need for end of treatment PET/CT. Also patients who achieved complete response on interim PET/CT may discontinue bleomycin from subsequent chemotherapy cycles due to balance of benefit vs risk of lung toxicity.
- Patients with equivocal (Deauville 3) response on interim PET/CT are to continue ABVD chemotherapy with end of treatment PET/CT reassessment.
- Patients with unsatisfactory response (Deauville 4 and 5) are to be considered for treatment with escalated BEACOPP with PET/CT scan reassessment after 2 cycles of escalated treatment. An end of treatment PET/CT will be required if no complete response achieved post 2 cycles of escalated BEACOPP chemotherapy.

Patients who remain PET-positive on completion of therapy may require re-biopsy with consideration of radiotherapy to residual disease and PET/CT scan re-assessment 3 months after radiotherapy.

Transplant eligible patients with primary refractory/progressive disease are to be offered salvage chemotherapy followed by high dose chemotherapy with autologous stem cell transplant.

Patients who are not fit for intensive chemotherapy are to be offered palliative treatment with steroids and/or weekly Vinblastine monotherapy and radiotherapy to symptomatic bulk of disease.

Nodular Lymphocyte Predominant Hodgkin Lymphoma

Patients with NLPHL stage IA who underwent diagnostic excision biopsy with no residual disease on PET/CT scan are to be considered for active monitoring.

Patients with residual but localized NLPHL (stage IA and IIA with ≤2 sites of disease) where the involved nodes are contiguous and can be safely encompassed within a radiation field are to be offered radiotherapy treatment.

Patients with stage IIA NLPHL who are not suitable for involved field radiotherapy are to be treated as advanced stage disease.

Patients with advanced stage NLPHL are to be offered 8 cycles of R-CVP chemotherapy.

Patients with advanced stage with a high index of suspicion of transformed disease are to be considered for 6 cycles of R-CHOP chemotherapy.

Response to treatment is to be assessed with repeated PET-CT scan after 4 cycles of chemotherapy with aim to continue chemotherapy up to the planned number of cycles - unless there is evidence of primary refractory/progressive disease on interim PET scan. Management primary

refractory/progressive NLPHL requires MDT discussion with highly individualized treatment approach.

Treatment of Relapsed Hodgkin Lymphoma

Relapsed disease is to be reassessed with PET/CT scan with repeat biopsy strongly recommended.

All relapsed cases of HL are to be discussed at the network MDT. Treatment decisions must be considered in the context of the patient's goals (palliative vs curative), performance status, transplant eligibility, previous treatments and response.

Transplant eligible patients are to be offered salvage chemotherapy (DHAP, IVE or ICE). After two cycles of salvage chemotherapy response to treatment is to be assessed with PET/CT scan. Responding patients are to be offered high dose chemotherapy with autologous stem cell transplantation.

Patients with unsatisfactory response to initial salvage chemotherapy are to be considered for alternative salvage regimen, Brentuximab, palliative treatment or clinical trial.

If autologous stem cell transplantation has not resulted in long lasting remission or if patient failed stem cell harvesting but being still fit enough for transplantation and suitable donor can be found - allogenic stem cell transplantation should be discussed with patient and transplant centre in Leeds or Sheffield.

Brentuximab vedotin, Pembrolizumab and Nivolumab are the treatment options for primary refractory or relapsed cHL to be used in accordance with the products registration characteristic and NICE approval.

Clinical Trials

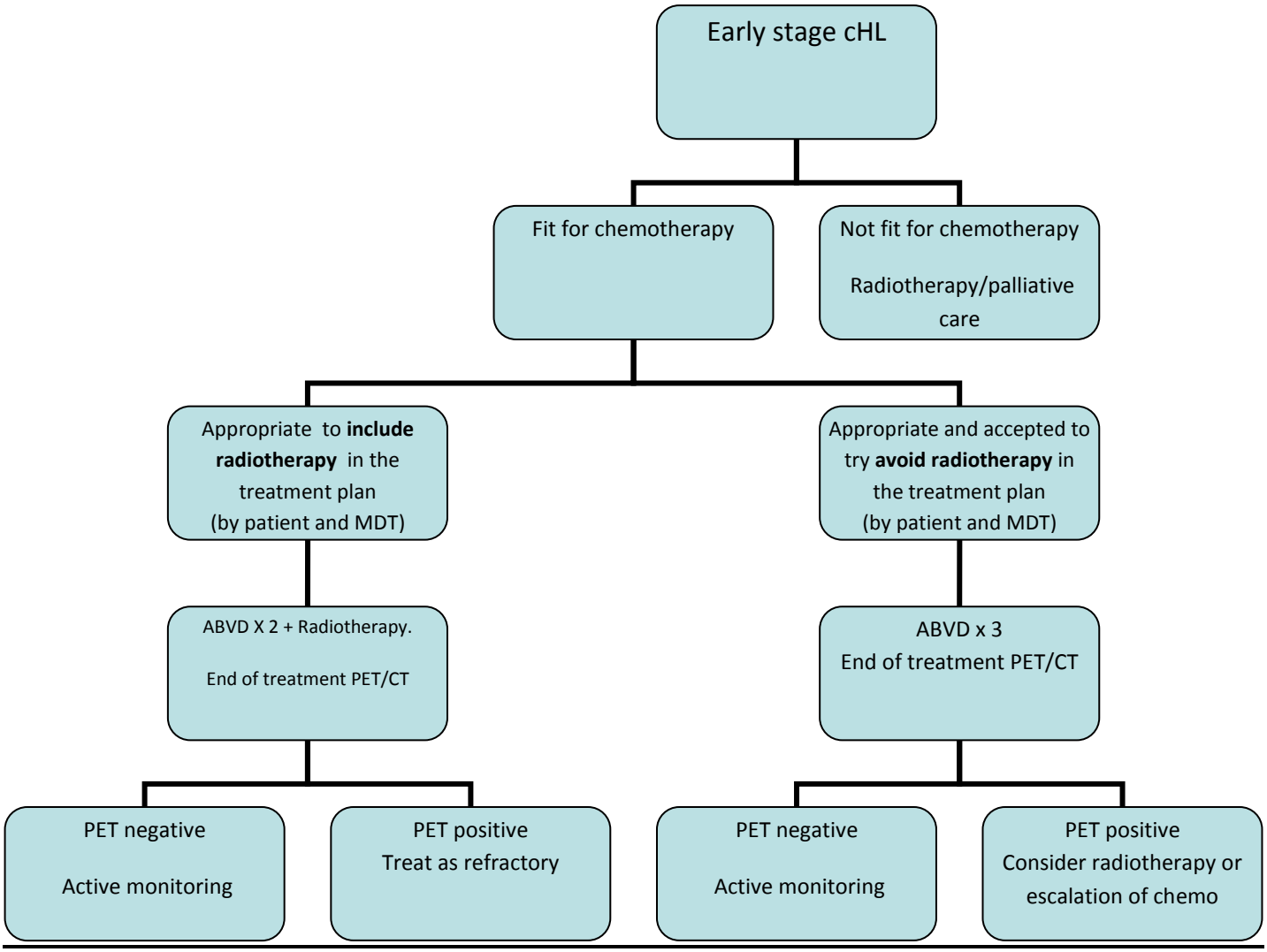
All patients should be considered for, and offered entry into clinical trials where available.

Palliative care services

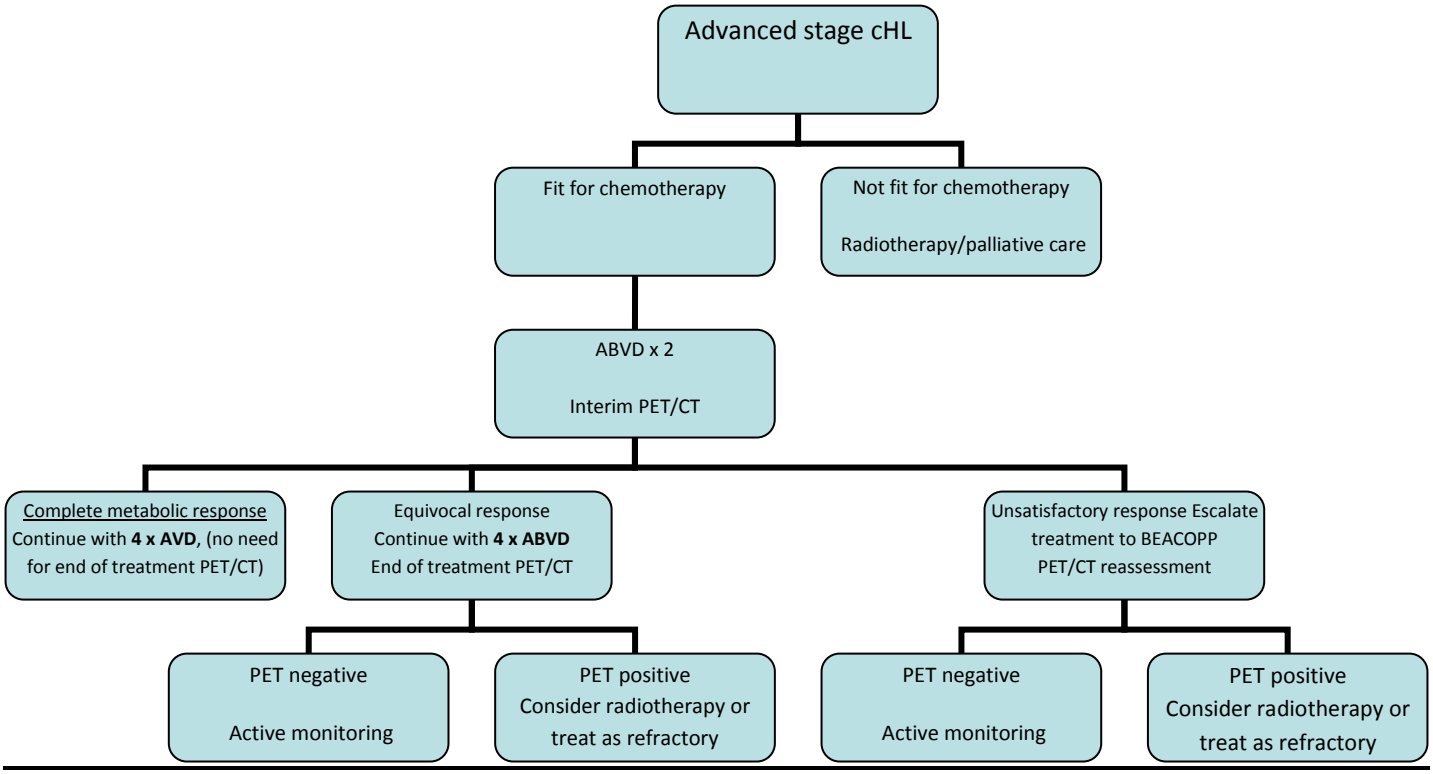
All Hodgkin Lymphoma patients will have a named key-worker who will undertake a holistic needs assessment and provide support and advice based upon this.

Referral to hospital or community palliative care services should be considered for patients unfit for chemotherapy and those with poor prognosis relapsed/refractory disease.

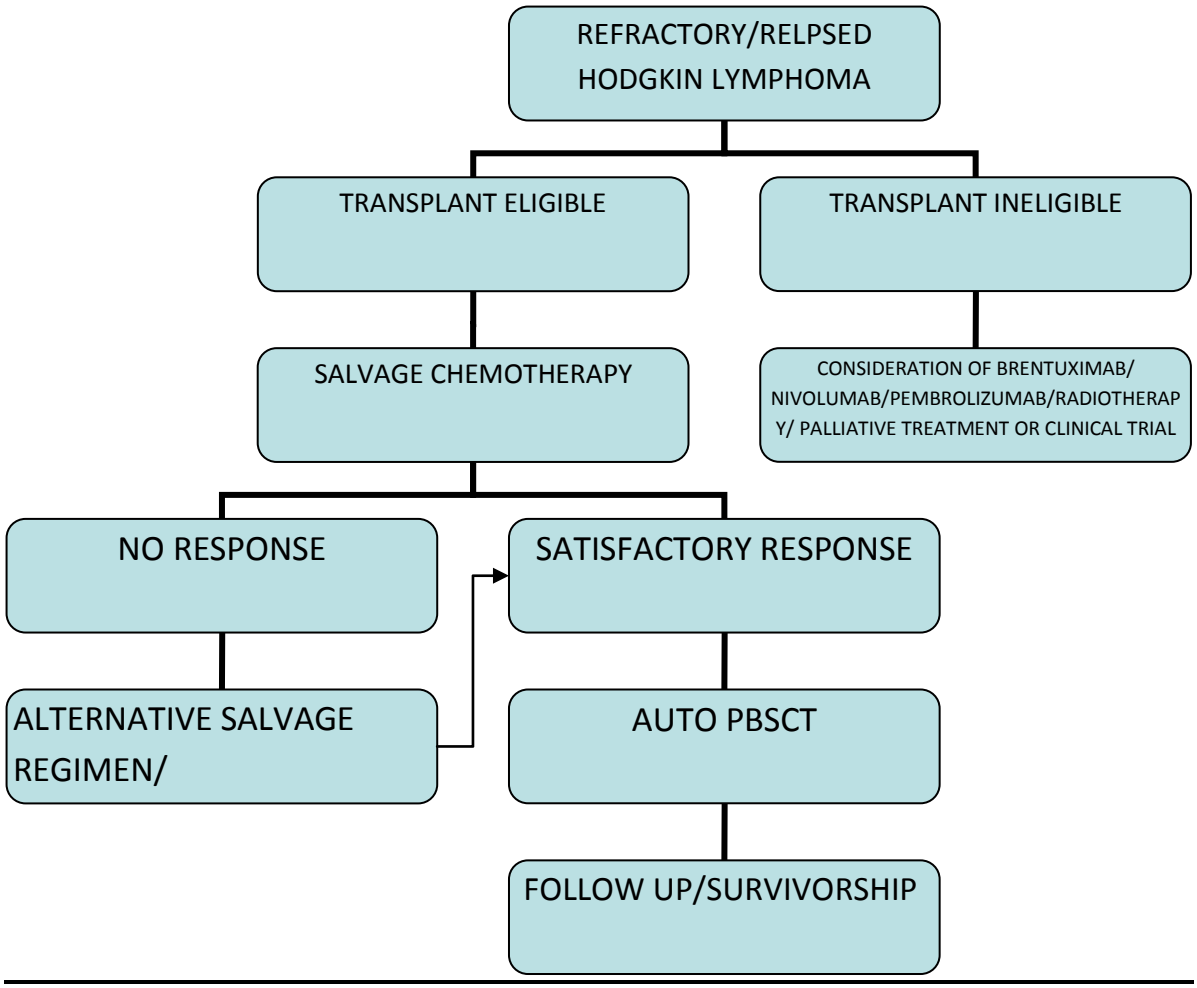
Patient Pathway, First line treatment, early stage Clasical Hodgkin Lymphoma



Patient Pathway, First line treatment, advanced stage Clasical Hodgkin Lymphoma



Patient Pathway, Refractory/Relapsed Hodgkin Lymphoma



3 PROCESS FOR MONITORING COMPLIANCE

Compliance will be audited within the MDT audit programme.

4 REFERENCES

- Hull and North Lincolnshire Haematology MDT operational policy September 2017.
- Haematological cancers: improving outcomes. NICE guideline [NG47] Published date: May 2016
- André MPE, Reman O, Federico M, Girinski T, Brice P, Brusamolino E et al. Interim Analysis of the Randomized EORTC/LYSA/FIL Intergroup H10 Trial On Early PET-Scan Driven Treatment Adaptation in Stage I/II Hodgkin Lymphoma. American Society of Hematology 2012 Annual Meeting. Abstract 549.
- Hasenclever D and Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. New Engl J Med 1998; 339: 1506-1514.
- Collins, G. P., Parker, A. N., Pocock, C. , Kayani, I. , Sureda, A. , Illidge, T. , Ardeshna, K. , Linch, D. C., Peggs, K. S. and , (2014), Guideline on the management of primary resistant and relapsed classical Hodgkin lymphoma. Br J Haematol, 164: 39-52. doi:10.1111/bjh.12582
- Follows, G. A., Ardeshna, K. M., Barrington, S. F., Culligan, D. J., Hoskin, P. J., Linch, D. , Sadullah, S. , Williams, M. V., Wimperis, J. Z. and , (2014), Guidelines for the first line management of classical Hodgkin lymphoma. Br J Haematol, 166: 34-49. doi:10.1111/bjh.12878
- McKay, P. , Fielding, P. , Gallop-Evans, E. , Hall, G. W., Lambert, J. , Leach, M. , Marafioti, T. , McNamara, C. and , (2016), Guidelines for the investigation and management of nodular lymphocyte predominant Hodgkin lymphoma. Br J Haematol, 172: 32-43. doi:10.1111/bjh.13842
- Radford J., Illidge T, Counsell N Results of a Trial of PET-Directed Therapy for Early-Stage Hodgkin's Lymphoma N Engl J Med 2015; 372:1598-1607 DOI: 10.1056/NEJMoa1408648, 2015
- Royal College of Physicians, The Royal College of Radiologists, Royal College of Obstetricians and Gynaecologists. The effects of cancer treatment on reproductive functions: Guidance on management. Report of a Working Party. London: RCP, 2007
- Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma

NICE guidance TA462, published 26/07/2017

- Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma
  NICE guidance TA446, published 28/06/2017

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