Version 2.2018
March 14, 2018

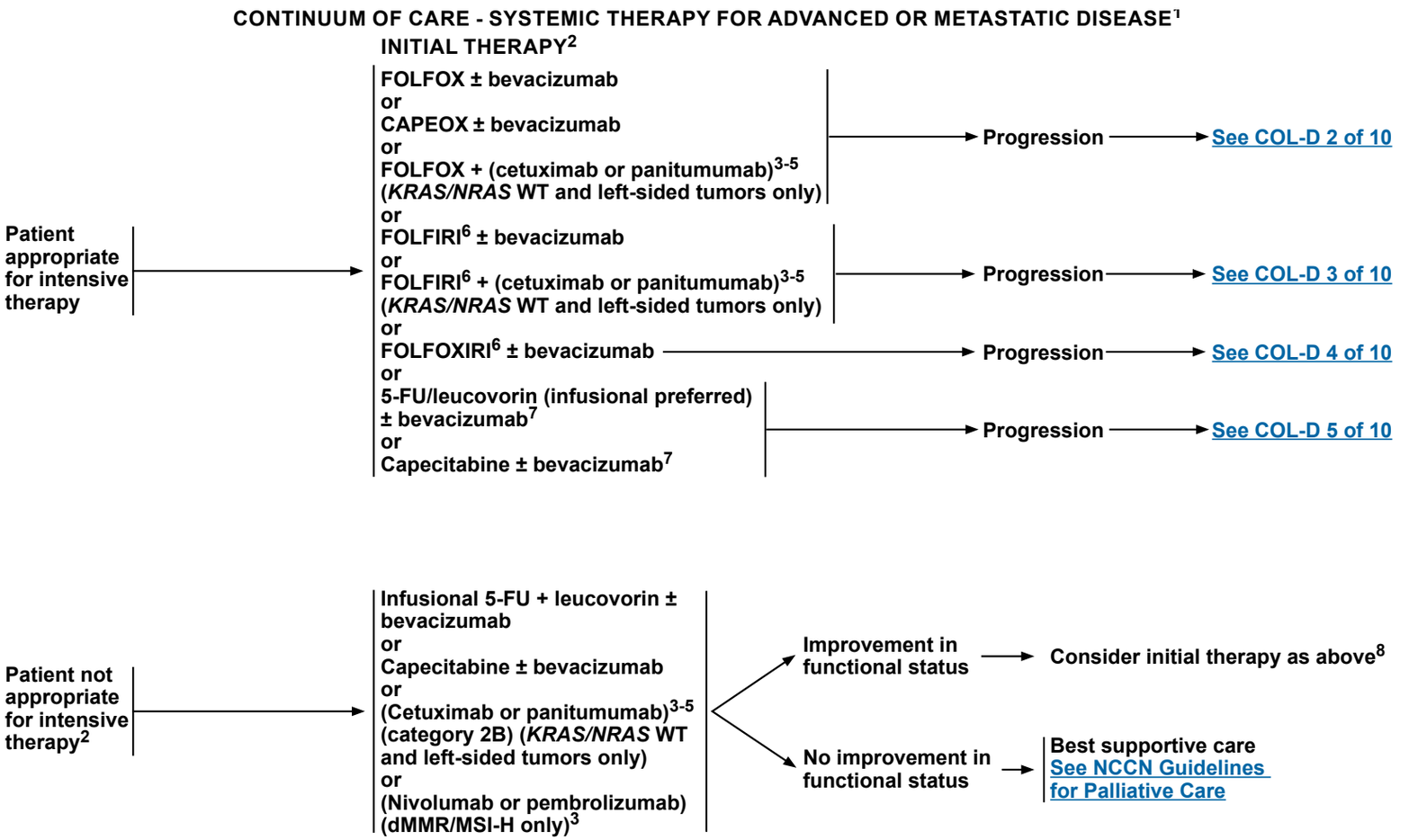
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Colon Cancer

Overall management of Colon Cancer from diagnosis through recurrence is described in the full NCCN Guidelines® for Colon Cancer. Visit NCCN.org to view the complete library of NCCN Guidelines.

National Comprehensive Cancer Network®

CONTINUUM OF CARE - SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE[1]



See footnotes COL-D 6 of 10

Note: All recommendations are category 2A unless otherwise indicated.
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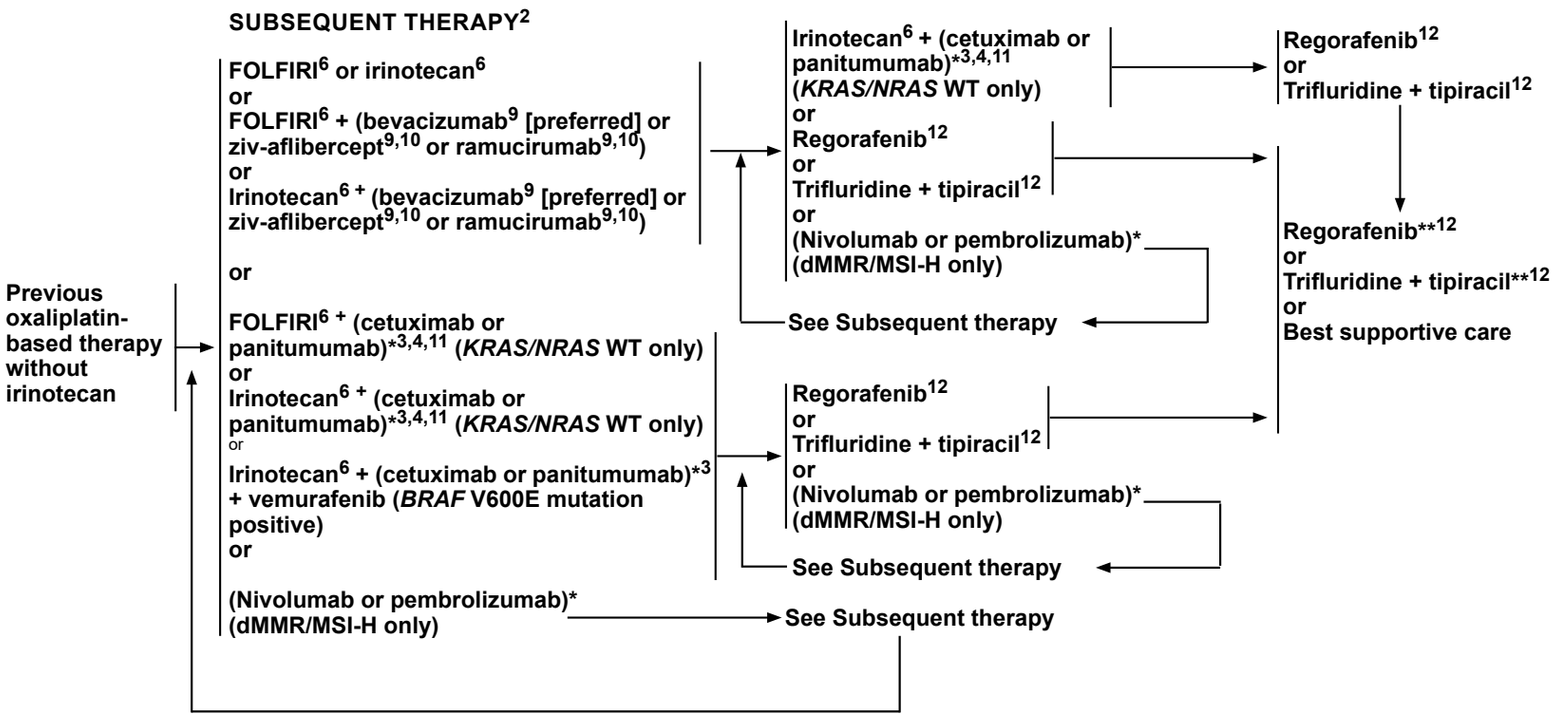

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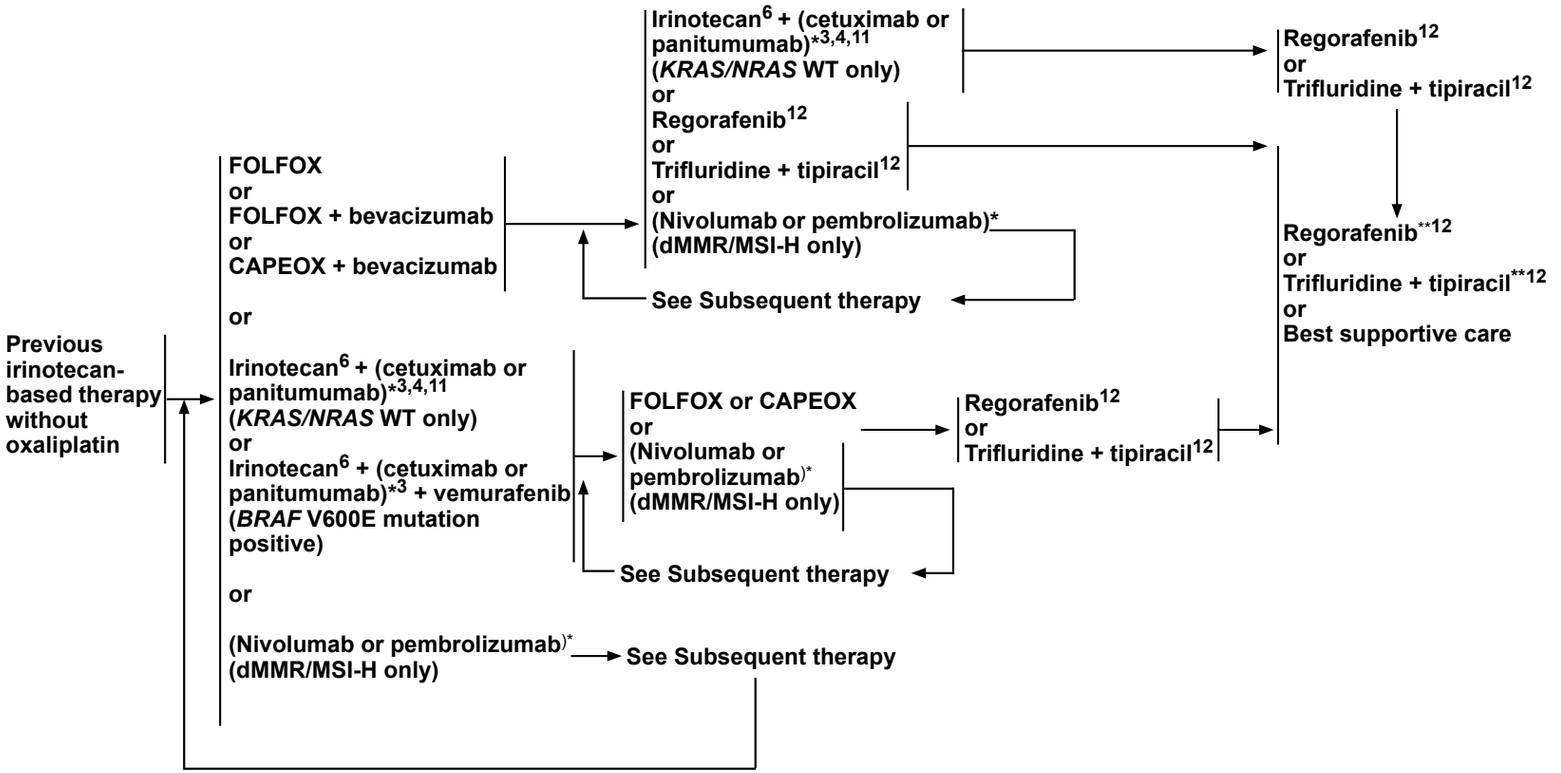
SUBSEQUENT THERAPY[2]



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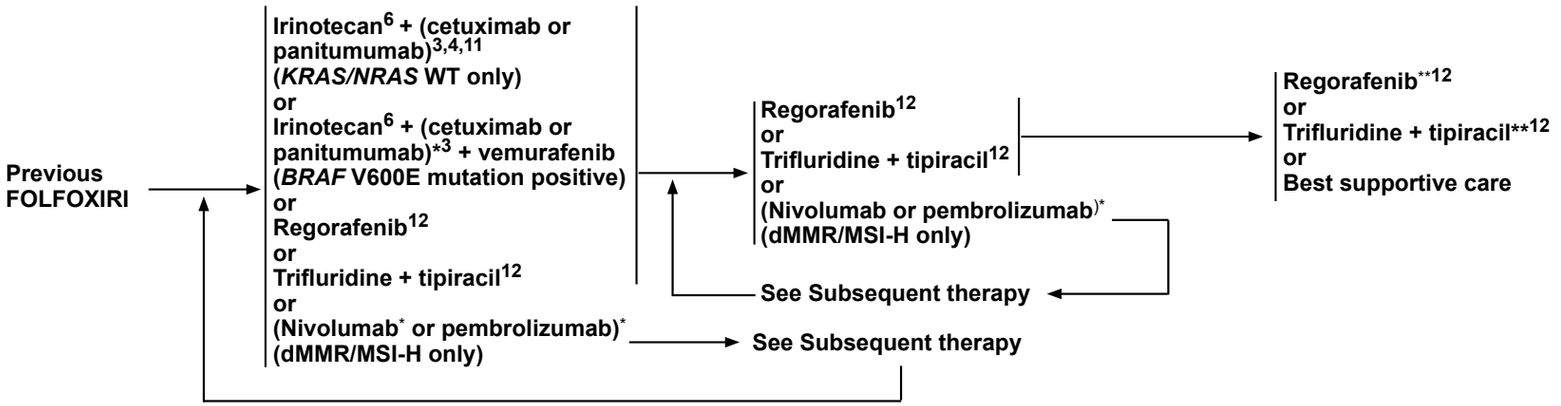

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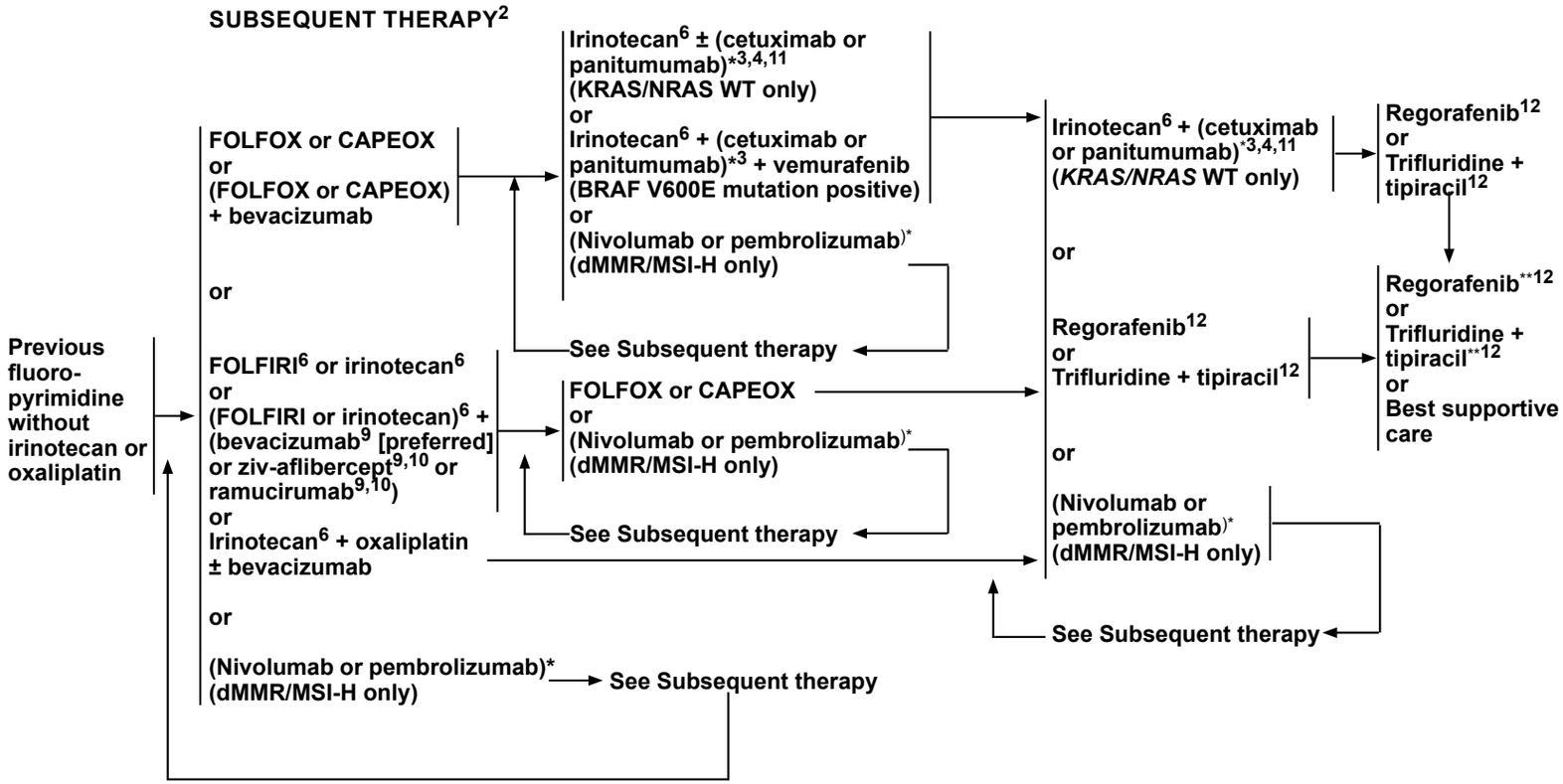

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SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE

[1]For chemotherapy references, see Chemotherapy Regimens and References (COL-D 7-10).
[2]Chest/abdominal/pelvic CT with contrast or chest CT and abdominal/pelvic MRI with contrast to monitor progress of therapy. PET/CT should not be used. See Principles of Imaging (COL-A).
[3]See Principles of Pathologic Review (COL-B 4 of 5).
[4]*BRAF* V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor.
[5]The panel defines the left side of the colon as splenic flexure to rectum. Evidence suggests that patients with tumors originating on the right side of the colon (hepatic flexure through cecum) are unlikely to respond to cetuximab and panitumumab in first-line therapy for metastatic disease. Data on the response to cetuximab and panitumumab in patients with primary tumors originating in the transverse colon (hepatic flexure to splenic flexure) are lacking.
[6]Irinotecan should be used with caution in patients with Gilbert's disease or elevated serum bilirubin. There is a commercially available test for *UGT1A1*. Guidelines for use in clinical practice have not been established.
[7]A treatment option for patients not able to tolerate oxaliplatin or irinotecan.
[8]The use of single-agent capecitabine after progression on a fluoropyrimidine-containing regimen has been shown to be ineffective; therefore, this is not recommended.
[9]Bevacizumab is the preferred anti-angiogenic agent based on toxicity and/or cost.
[10]There are no data to suggest activity of FOLFIRI-ziv-aflibercept or FOLFIRI-ramucirumab in a patient who has progressed on FOLFIRI-bevacizumab, or vice versa. Ziv-aflibercept and ramucirumab have only shown activity when given in conjunction with FOLFIRI in FOLFIRI-naïve patients.
[11]Cetuximab or panitumumab are recommended in combination with irinotecan-based therapy or as single-agent therapy for patients who cannot tolerate irinotecan.
[12]Regorafenib or trifluridine + tipiracil are treatment options for patients who have progressed through all available regimens.

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SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE - CHEMOTHERAPY REGIMENS (PAGE 8 of 10)

FOLFIRI + cetuximab (*KRAS/NRAS* WT only)
Cetuximab 400 mg/m^2 IV over 2 hours first infusion, then 250 mg/m^2 IV over 60 minutes weekly[12]
or Cetuximab 500 mg/m^2 IV over 2 hours, day 1, every 2 weeks[13]

FOLFIRI + panitumumab[14] (*KRAS/NRAS* WT only)
Panitumumab 6 mg/kg IV over 60 minutes, day 1
Repeat every 2 weeks

FOLFIRI + ziv-aflibercept[15]
Ziv-aflibercept 4 mg/kg IV over 60 minutes, day 1
Repeat every 2 weeks

FOLFIRI + ramucirumab[16]
Ramucirumab 8 mg/kg over 60 minutes, day 1
Repeat every 2 weeks

FOLFOXIRI[17]
Irinotecan 165 mg/m^2 IV day 1, oxaliplatin 85 mg/m^2 IV day 1,*
Leucovorin 400 mg/m^2 day 1, fluorouracil 1600 mg/m^2/d x 2 days (total 3200 mg/m^2 over 48 hours) continuous infusion starting on day 1.**
Repeat every 2 weeks
The dose of 5-FU listed here was used in European studies. U.S. patients have been shown to have poorer tolerance for 5-FU. A starting dose of 5-FU consistent with the dose recommended in FOLFOX or FOLFIRI should be strongly considered for U.S. patients.

FOLFOXIRI + bevacizumab[18]¶
Bevacizumab 5 mg/kg IV, day 1
Repeat every 2 weeks

IROX[19]
Oxaliplatin 85 mg/m2 IV,*
followed by irinotecan 200 mg/m^2 over 30–90 minutes every 3 weeks

Bolus or infusional 5-FU/leucovorin
Roswell Park regimen[20]
Leucovorin 500 mg/m^2 IV over 2 hours, days 1, 8, 15, 22, 29, and 36
5-FU 500 mg/m^2 IV bolus 1 hour after start of leucovorin, days 1, 8, 15, 22, 29, and 36
Repeat every 8 weeks

Simplified biweekly infusional 5-FU/LV (sLV5FU2)[9]
Leucovorin 400 mg/m^2 IV over 2 hours on day 1, followed by 5-FU bolus 400 mg/m^2 and then 1200 mg/m^2/d x 2 days (total 2400 mg/m^2 over 46–48 hours) continuous infusion**
Repeat every 2 weeks

Weekly
Leucovorin 20 mg/m^2 IV over 2 hours on day 1, 5-FU 500 mg/m^2 IV bolus injection 1 hour after the start of leucovorin. Repeat weekly.[21]
5-FU 2600 mg/m^2 by 24-hour infusion plus leucovorin 500 mg/m^2
Repeat every week[21]

See References on COL-D 10 of 10

*Oxaliplatin may be given either over 2 hours, or may be infused over a shorter time at a rate of 1 mg/m^2/min. Leucovorin infusion should match infusion time of oxaliplatin. Cercek A, Park V, Yaeger R, et al. Faster FOLFOX: oxaliplatin can be safely infused at a rate of 1 mg/m^2/min. J Oncol Pract 2016;12:e548-553.
**Leucovorin 400 mg/m^2 is the equivalent of levoleucovorin 200 mg/m^2.
¶Bevacizumab may be safely given at a rate of 0.5 mg/kg/min (5 mg/kg over 10 minutes and 7.5 mg/kg over 15 minutes).

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